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BINAURAL INTERACTION IN THE ACCESSORY SUPERIOR OLIVARY NUCLEUS OF THE CAT—AN ELECTROPHYSIOLOGICAL STUDY OF SINGLE NEURONS

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Abstract

In an effort to understand the neural encoding of binaurally presented stimuli, clicks were presented through earphones to the two ears of Dial-anesthetized cats. The electrical response activity of single nerve cells in the accessory nucleus of the superior olive was studied. Stimulus parameters investigated include interaural time difference, interaural intensity difference, and average intensity. Attention was focused on cells that were excited by stimulation of the contralateral ear and inhibited by stimulation of the ipsilateral ear. These cells may be thought of as logical transducers that convert stimulus differences at the two ears into patterns of response activity which can be "read" by higher neural centers. A model by which judgments of image localization are obtained on the basis of patterns of activity in the accessory nuclei is suggested. In the model, the position of the fused virtual image is determined by a comparison of the amount of response activity in the left and right accessory nuclei. Incorporation of empirical data into the model yields predictions that are in quantitative agreement with results of human psychophysics. The model predicts that the virtual image should be localized toward the side receiving more intense or prior stimulation. A time-intensity trading relationship is derived which is in quantitative agreement with the time-intensity trading relationship obtained in psychophysical "centering" experiments. A statistical treatment of the data predicts minimum detectable changes in interaural time difference of 5-10 μsec, and minimum detectable changes in interaural intensity difference of 0.1-0.5 db.

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I. INTRODUCTION

One of the important ways in which organisms, including man, gain information about their environment is by means of the auditory localization of sound stimuli. If a source of sound is located to one side of an observer, the sound waves have a longer distance to travel to reach the ear on the opposite side than to reach the ear on the nearer side, so that there results a difference in time of arrival of the stimuli at the two ears. Furthermore, the observer's head produces a "shadowing" effect, thereby reducing the intensity of the stimulus at the ear on the opposite side, so that there results a difference in the intensity of the stimuli at the two ears. This "shadowing" effect is more pronounced at high frequencies than at low, so that for complex stimuli there results a difference in spectral content of the stimuli at the two ears. These factors, interaural time difference, interaural intensity difference, and difference in spectral content of the stimuli at the two ears, are included among the physical parameters that are available to the observer in determining the position of a source of sound.

There has been much conjecture as to the neural mechanisms involved in the localization of a source of sound. Numerous models have been proposed, based primarily on the results of psychophysical experiments on humans. A handicap of such model building has been the lack of adequate pertinent data on the anatomical structures and electrophysiological mechanisms involved. The electrical activity evoked in the central nervous system by binaurally presented pairs of stimuli has been investigated, but in most studies either the interaural time differences involved were large compared with the interaural time differences resulting from free-field stimulation or the activity observed could be interpreted as an indication that interaction between the stimuli to the two ears had its origin at some more peripheral level.

We investigated the electrical activity of single nerve cells in the accessory nucleus of the superior olive in cats, using as stimuli acoustic clicks presented to the two ears through earphones. The stimulus parameters investigated were interaural time difference, interaural intensity difference, and average intensity. From our data we inferred relationships of these parameters to statistics of response activity in the two accessory nuclei. Through a simple model we relate these statistics of response activity in cats to human judgments of the position of the apparent sound source. The resulting predictions are compared with available psychophysical data.

We presented the stimuli through earphones in order to make possible the independent manipulation of interaural time and intensity difference. When this procedure is used in psychophysical experiments on humans, the subject usually reports that the sound source appears to be located inside his head. This is referred to in psychophysical terminology as lateralization, as opposed to the localization of free-field stimuli. There is some indication that this phenomenon is caused in part by the effects of head movements, in part by the fact that the combinations of interaural time and intensity differences do not correspond to free-field situations, and in part to more subtle,

subjective factors – factors such as the subject's expectation as to where the sound source should be located. It is generally accepted that lateralization can be regarded as a special case of localization.

Implicit in our use of results of electrophysiological experiments on cats to obtain predicted judgments which we then compare with results of psychophysical experiments on humans is the assumption that cat and man are comparable. This assumption is to some extent forced on us because of the necessity of having a laboratory preparation in which we can observe activity of single nerve cells and because the bulk of data on the anatomy of the central auditory pathway in mammals is based on studies of the cat. There is evidence from behavioral experiments on cats which indicates that cat and man are capable of approximately the same degree of precision in tasks requiring the auditory localization of sounds in space.

The choice of the accessory nucleus of the superior olive as a level of the central nervous system for our electrophysiological investigations was made on both electrophysiological and anatomical grounds. There is anatomical and electrophysiological evidence that indicates that the accessory nucleus is the most peripheral station in the classical ascending auditory pathway to receive innervation from both ears. Microelectrode studies have demonstrated the existence of units in the accessory nucleus which reflect by their activity small changes in interaural time difference.

We were faced with the problem of obtaining meaningful results by observing the activity of a small number of cells out of a very large population of cells. There was the additional consideration that, because of pulsation of the brain and possible injury to cells, we could not be assured of holding an individual cell for observation for a long period. These factors led to our decision to severely restrict the number of stimulus parameters and to investigate these parameters as thoroughly as possible.

On the basis of our data we suggest an idealized mathematical model relating statistics of neural activity to judgments of localization of binaural click stimuli. It is possible that in the future, as a result of further experimentation, the model may be generalized to encompass a much wider range of stimuli, but here we shall confine our discussion to the more restricted context. For the limited range of stimulus parameters considered in this report, results of human psychophysics seem to parallel predictions of the model which are derived from electrophysiological experiments on cats.

II. ANATOMY OF SUPERIOR OLIVE

The anatomy of the central auditory pathway in the region of the superior olive is extremely complex, and at best incompletely understood. Electrophysiological studies indicate the existence of interconnections that have not been observed anatomically, and there are unresolved contradictions among various anatomical studies.

We present here a summary of the most pertinent material relating to the region of the superior olive, based primarily on studies of cat. We discuss the gross structure of the superior olivary complex, the cellular composition of the accessory nuclues of the superior olive, the afferent input to the accessory nucleus, and the efferent output from the accessory nucleus.

2.1 GROSS STRUCTURE OF THE SUPERIOR OLIVARY COMPLEX

The superior olivary complex is a bilaterally symmetrical structure (see Fig. 1), each half of which is generally considered to be composed of five distinct cellular groups. There are other cellular groups that may or may not be considered to be included in the superior olivary complex.[1-8]

The two most distinct components in cats are the S-shaped segment (lateral nucleus of the superior olive, superior olive proper), and the accessory nucleus (medial nucleus of the superior olive, paraolivary nucleus of Winkler). Ventral to these are the internal and external preolivary nuclei (medial and lateral preolivary nuclei, lateral trapezoid nucleus of Winkler). Medial to the preolivary nuclei is the nucleus of the trapezoid body.

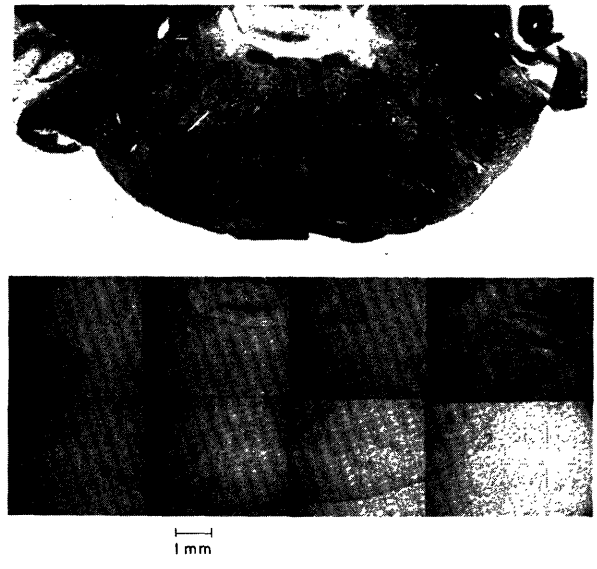


Fig. 1. Gross structure of the superior olivary complex. 20-μ sections through the ventral portion of the brain stem. Top, Weil stain, showing fibers. Bottom, Cresyl violet stain, showing cell bodies.

Lesser subdivisions of the superior olivary complex include the dorsal and ventral nuclei of the lateral lemniscus, which appear as the rostral extension of the preolivary nuclei, and a group of cells in the dorsal, rostral region of the accessory nucleus giving rise to the olivocochlear pathway.

The lateral superior olivary nucleus consists of a compact gray lamina. This lamina is folded so that it appears in transverse section as having an S shape, with the more medial loop directed dorsally, and the other ventrally. The medial limb is larger and longer than the lateral limb. This nucleus is situated just dorsal to the fibers of the trapezoid body, with the ventral loop resting on the external preolivary nucleus.

The principal afferents to the lateral nucleus appear to come from the ipsilateral cochlear nucleus, and the efferents in the main to be divided equally between the ipsilateral and contralateral lateral lemnisci.[1,8] These are not the only connections of the S-shaped segment, since the medial limb is connected by cell strands to the external preolivary nucleus.[5] The function of these fibers is not clear.

This nucleus, interestingly, is hypertrophied in micro-ophthalmic animals, and is rudimentary in primates.[5]

The accessory nucleus of the superior olive is situated medial to the S-shaped segment. Its lateral surface touches the S-shaped segment, and its ventral surface indents the mass of transverse fibers of the trapezoid body. It is not folded as is the S-shaped segment, but rather appears as a broad, elongated plate, with its largest dimension, approximately 6 mm,[2,8] in the rostral-caudal direction. It is roughly crescent-shaped, the medial surface convex and the lateral surface concave. It is narrowest caudally, becoming larger rostrally, with a representative dorsal-ventral measure of 2 mm.

The cell structure and connections of the accessory nucleus are considered in a separate section.

The internal and external preolivary nuclei are located ventral to the lateral S-shaped segment. These two nuclei lack definite form, since they are pierced through by fiber bundles of the trapezoid body. The two nuclei are separate caudally, but rostrally they fuse to join the nuclei of the lateral lemniscus.[5]

The main afferents to the internal and external preolivary nuclei appear to come from the ipsilateral ventral cochlear nucleus.[8] The efferent projections from both nuclei appear to be predominantly into the ipsilateral lateral lemniscus.[8] There are also collaterals between the external preolivary nucleus and the lateral S-shaped segment, and between the internal preolivary nucleus and the accessory nucleus.[5]

The nucleus of the trapezoid body is located medial and ventral to the accessory nucleus and dorsal to the fiber bundles of the trapezoid body. The connections to this nucleus are not well understood: According to one study it receives afferents from the contralateral cochlear nucleus only.[8] Other authors suggest that it receives homolateral afferents as well.[3] Its efferent projections are not clear.

The nuclei of the lateral lemniscus are not generally considered to be part of the superior olivary complex, but there seems no justification for making a clear-cut

distinction. They consist of two cell groups, dorsal and ventral, located in the course of the lateral lemniscus. The ventral group is located dorsal and lateral to the S-shaped segment and appears as the dorsal extension of the preolivary nuclei. The afferent supply to these nuclei appears to come mainly from the contralateral ventral cochlear nucleus, and to come very little if at all from fibers originating in the olivary complex.[7,8]

One final nucleus that might be included in this gross description of the superior olivary complex is a group of cells located dorsal and medial to the accessory nucleus. This group of cells gives rise to the efferent olivocochlear pathway, which terminates in the contralateral cochlea. Little is known about the afferent connections to this cell group, and it is unclear whether it should be considered as a distinct nucleus or as part of the accessory nucleus.[1]

2.2 CELL STRUCTURE OF THE ACCESSORY NUCLEUS

The previous section constituted a gross description of the composition of the superior olivary complex. Since we are particularly concerned with the accessory nucleus, we are treating the cell structure and fiber connections of this nucleus in separate sections.

Our knowledge of the cell structure and characteristic synaptic endings of the accessory nucleus stems largely from the work of Ramon y Cajal.[6] More recent contributions have been made by Rasmussen[7] and by Stotler.[8]

The accessory nucleus consists of a flattened bar, with its length running rostrally to caudally and its breadth extending dorsomedially to ventrolaterally. Of the various cell types in the accessory nucleus (see Fig. 2), the ones that appear to be most numerous are the ones in which we are particularly interested. The bodies of these cells are large, approximately 30 μ long, and are spindle-shaped.[6,8] At each pole they are prolonged into two, three, or more dendrites. These dendrites run generally perpendicular to the length and breadth of the nucleus. Each cell emits an axon perpendicular to the cell body. The axon occasionally may be displaced toward one or the other dendritic pole. The cells themselves are arranged in four or five irregular parallel layers, and these layers are held somewhat separated from each other by very abundant neuropil.[6,8]

The dendrites terminate near the margins of the nucleus. Dendrites originating on the lateral pole of the cell appear to terminate on the lateral margin of the nucleus; dendrites originating on the medial pole of the cell appear to terminate on the medial margin of the nucleus. The dendrites terminate in a cluster of short, thorny branches, with shredded and very uneven contours.

The junction between the dendrites and the afferent fibers is, from Ramon y Cajal's description, extremely intimate. Afferent fibers come in at the edges of the nucleus, at the termination of the dendrites, run roughly parallel to the dendrites, and finally cover the cell body. As the afferent fibers get closer and closer to the cell body, they get finer and finer, while the dendrites get coarser and coarser. All along the way there are numerous connections between the afferent fibers and the dendrites, and the

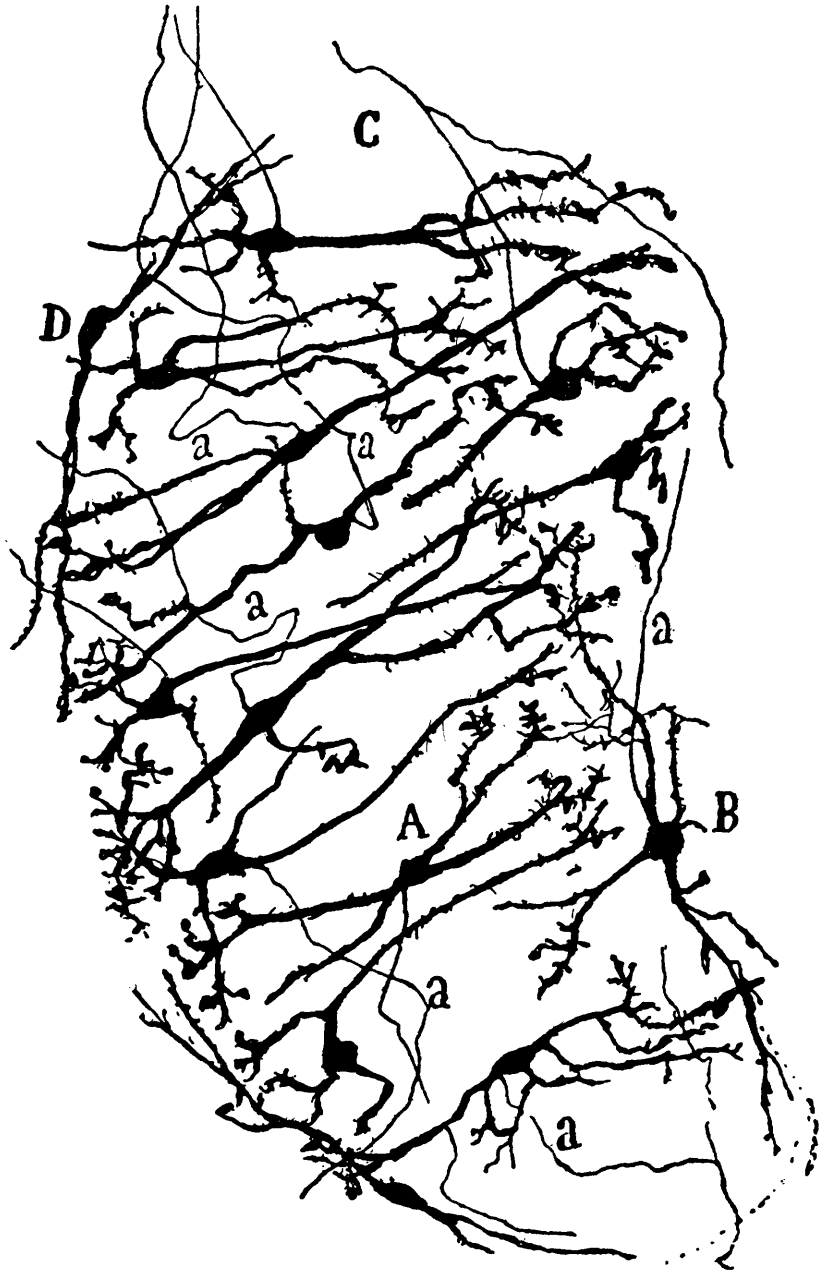


Fig. 2. Cell structure of the accessory nucleus as given by Ramon y Cajal.[9]

afferent fibers send off branches to neighboring dendrites. The end result is that the cell body is covered by a plexus of nerve fibers, so fine and attached so intimately to the cell body that it gives the appearance of a membrane. The plexus surrounding a given cell arises from many afferent fibers, and a given afferent fiber contributes to the plexuses surrounding many cells.[6]

Although the cell type described above is the most frequent, there are others. Ramon y Cajal describes cells that are also spindle-shaped and quite large, but are situated along the margins of the accessory nucleus. The course of the dendrites of

these cells is not clear, but they appear to pass parallel to the nucleus and to emerge through the boundary at which the cell is located.[6] Also, cells that are characteristic of the trapezoid nucleus are found in the most caudal region of the accessory nucleus.[2]

2.3 AFFERENT SUPPLY TO THE ACCESSORY NUCLEUS

Our knowledge of the afferent supply to the accessory nucleus of the superior olive comes first from the work of Ramon y Cajal[6] and from recent contributions by Stotler.[8] We must also consider observations made by Papez[5] and by Lewy and Kobrak,[3] which provide some evidence in conflict with observations made by Stotler.

It is clear that both ears are represented at the accessory nucleus. The origin of the afferent fibers and their specific termination is less well established. Ramon y Cajal describes two groups of afferent fibers, both coming as collaterals or terminals from the trapezoid body. According to Ramon y Cajal, the majority of afferents enter the accessory nucleus by the medial side, and the remaining afferents slide between the ventral loop of the S-shaped segment and the accessory nucleus by the lateral side. It appears from later work,[8] as we shall discuss, that the group entering the accessory nucleus by the medial side represents the contralateral ear and the group entering the accessory nucleus by the lateral side represents the ipsilateral ear.

These are probably not the only afferents to the accessory nucleus. The ventral border of the accessory nucleus is connected by cell strands to the internal preolivary nucleus,[5] and a descending pathway terminates in the region of the cells giving rise to the efferent olivocochlear pathway.[1] The origin of fibers of the trapezoid body, which might possibly contribute to the innervation of the accessory nucleus, is unclear. Stotler found, in Marchi degeneration studies, that severing the cochlear nerve from the spiral ganglion produced degeneration restricted to the ventral cochlear nucleus, with no degeneration in the trapezoid nucleus or superior olivary complex. This suggested to Stotler the absence of primary representation above the level of the ventral cochlear nucleus. Lewy and Kobrak, on the other hand, report the existence of fibers, originating at the cochlea, which branch into the trapezoid body and end near the contralateral nucleus of the trapezoid body. This primary projection, according to Lewy and Kobrak, is strongest from the apical turn of the cochlea.

While the evidence for primary representation at the level of the superior olivary complex is ambiguous, the origin of the main afferent supply is well established. Cells in the ventral cochlear nucleus project through the trapezoid body, to end on the ipsilateral and contralateral accessory nuclei.[1,3,8] These projections appear to comprise the two afferent pathways observed by Ramon y Cajal and described above. In this way, each ear is represented at least by second- or higher-order fibers at the accessory nucleus.

The mode of termination of these fiber tracts upon the cells of the accessory nucleus is particularly interesting. Stotler[8] found that if the cochlear nucleus is severed from the brain stem, the neuropil surrounding the lateral pole of cells in the ipsilateral

accessory nucleus degenerates, and the neuropil surrounding the medial pole of cells in the contralateral accessory nucleus degenerates. Stotler took this to indicate that individual cells in the accessory nucleus receive innervation from both ears. This property is exactly what would be required of cells involved in making fine discriminations of interaural time and intensity difference.

2.4 EFFERENTS FROM THE ACCESSORY NUCLEUS

There are numerous efferents from the accessory nucleus, including continuations of the classical ascending pathway, reflex connections to various motor nuclei, and descending tracts. Here again, published observations are incomplete and at times contradictory.

The accessory nucleus projects along the classical ascending pathway through the lateral lemniscus. It is likely that these fibers go at least as far as the inferior colliculus without interruption.[8] There is disagreement as to whether the accessory nucleus projects through both the ipsilateral and contralateral lateral lemnisci. Stotler reports that all cells of the ipsilateral accessory nucleus react to destruction of the inferior colliculus. This he takes to indicate that the accessory nucleus projects only through the ipsilateral lateral lemniscus. Rasmussen, on the other hand, claims that the accessory nucleus projects through both lemnisci. Furthermore, he indicates that some of these fibers synapse at the ventral and dorsal nuclei of the lateral lemniscus. We might point out that while the Marchi degeneration method used by Stotler is sufficient for demonstrating the presence of fiber connections, it is not sufficient for demonstrating their absence.

Fibers from the accessory nucleus go to various motor reflex centers. These connections are not known in detail. Motor functions possibly involved include movement of the head and neck, contraction of middle-ear muscles, and movement of the eyes.[7]

There is also a large descending tract, the olivocochlear pathway, originating at or near the accessory nucleus. This tract terminates in the region of the contralateral cochlea. It is believed to exercise inhibitory control at the periphery.[10,11]

III. ELECTROPHYSIOLOGICAL EVIDENCE OF BINAURAL INTERACTION

There is clear evidence of interaction between neuroelectric responses evoked by the two ears at every level of the auditory pathway above the superior olivary complex, but not peripheral to the superior olivary complex (see Fig. 3). It should be borne in

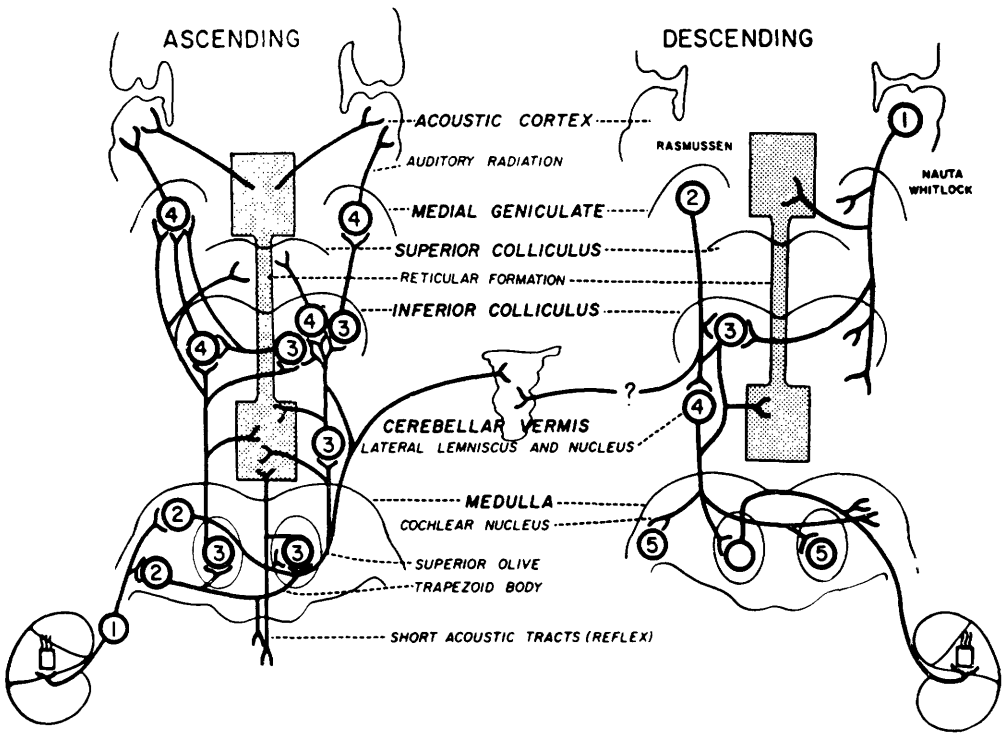


Fig. 3. Diagram of auditory pathways in a typical mammalian brain as given by R. Galambos.[13]

mind that most studies to date have been performed on acute, deeply anesthetized preparations. In these preparations, the activity of the central nervous system, including the descending pathways mentioned above, could be expected to be profoundly affected by the anesthetic.

3.1 BINAURAL INTERACTION PERIPHERAL TO THE SUPERIOR OLIVE

Most available evidence argues against the existence of binaural interaction peripheral to the superior olivary complex in the classical ascending pathway. This is not surprising, since the earliest opportunity for convergence of fibers from the two ears in the classical ascending pathway appears to be at the superior olive.

Binaural interaction at the periphery has been reported in one case.[12] The response observed at the round window appeared to be modified by stimulation of the contralateral ear. This phenomenon proved to be ephemeral, however, and may have been due to electrotonic spread.

Rosenzweig and Amon[14] looked for binaural interaction at the cochlear nucleus, using the following criterion: Interaction was said to have occurred if the response evoked when the two ears were stimulated together differed from the sum of responses evoked when the two ears were stimulated separately. They found no interaction at the cochlear nucleus.

3.2 INTERACTION AT THE LEVEL OF THE SUPERIOR OLIVE

Our knowledge of binaural interaction at the superior olive comes primarily from gross-response work by Rosenzweig et al.,[14-16] single-unit work by Galambos et al.[2] and Schwartzkopff,[17] and preliminary reports by Moushegian and Rupert.[18]

Rosenzweig and Amon, using their criterion of interaction described above, compared the response evoked by stimuli delivered to both ears with the sum of responses evoked by stimulating the two ears separately with the same stimuli.[14] It is impossible to tell just where their electrodes were, but they do say that interaction occurs at most locations in the superior olivary complex and at some locations at the midline of the trapezoid body. The response observed in the superior olivary complex and in the trapezoid body typically had a peak latency of approximately 4 msec.

Galambos' observations on binaural interaction in single units in the accessory nucleus[2] are few, but extremely provocative. These observations were instrumental in suggesting the present investigation. Galambos describes units whose responsiveness is influenced by extremely small differences of interaural time delay. The one unit described in detail never responded when the stimulus to the right ear preceded the stimulus to the left ear by 0.5-1.1 msec and always responded when right preceded left by less than 0.2 msec or more than 1.7 msec. The time over which suppression of response occurred apparently did not depend on the relative intensities of the stimuli at the two sides. While it is difficult to determine the latency of this unit from their figures, it appears that the latency was approximately 5-10 msec. Galambos states that this unit "always responded to clicks presented monaurally to the right ear, and never to monaural left clicks."[19]

Galambos states that four units that exhibited such behavior were observed, all in the accessory nucleus. The small number of units may be explained by the fact that Galambos was not interested primarily in binaural interactions.

Units in the accessory nucleus that are excited by a stimulus delivered to one ear and inhibited by a stimulus delivered to the other ear have also been described by Moushegian and Rupert.[18] They report that latency of response for these cells is influenced by the interaural time difference. The responsiveness, as measured by the number of responses occurring to repetitions of the stimulus, is also affected.

3.3 INTERACTION CENTRAL TO THE SUPERIOR OLIVE

Since interaction has been found to occur at the level of the superior olivary complex, it is not surprising that it has also been found at all higher levels.

Kemp and Robinson found little, if any, interaction at the lateral lemniscus,[20] and interpreted this to argue against the possibility of convergence of fibers from the two ears at the cochlear nucleus or superior olivary complex. This influenced thinking on the problem of localization of sounds in space for many years.

More recently, however, Rosenzweig did find evidence of binaural interaction at the lateral lemniscus.[14,15] The response that he observed was extremely complex and was a strong function of position of the recording electrode. Different components of the response showed different amounts of binaural interaction. Because the lateral lemniscus is composed of fibers from many different levels, this seems quite reasonable.

Binaural interaction in single cells of the inferior colliculus has been observed by both Erulkar[21] and Hind, Goldberg, Greenwood, and Rose.[22] Some cells in the inferior colliculus are excited by stimulation of either ear, and, if stimuli are presented to both ears within a few milliseconds, these cells may exhibit summation. Other cells are excited by stimulation of one (usually the contralateral) ear and inhibited by stimulation of the other ear.

3.4 INTERACTION AT THE AUDITORY CORTEX

Each ear is represented at the auditory cortex. A stimulus presented to the left ear, for example, evokes a response at both the left and right hemispheres. The representation of one ear at the two sides of the cortex is not identical, and is a function of the stimulus presented to the other ear.

Over a wide range of intensities, a stimulus presented to one ear evokes a larger response at the contralateral side of the cortex than at the ipsilateral side.[23-25] Thus, even in the absence of interaction, interaural difference of intensity would appear at the cortex as unequal size of response at the two sides.

Differences between the responses at the two sides of the cortex result not only from differences in interaural intensity but also from differences in time of arrival of the stimulus at the two ears.[23] For this to result, there must be interaction between responses to the two stimuli, since the effective interaural time differences are small compared with the times involved in the cortical response. This interaction does occur, and is seen most clearly if the response evoked by two stimuli delivered simultaneously to the two ears is compared with the sum of the responses evoked by the same two stimuli delivered separately. The response in the first case is smaller than the sum of responses in the second case.[24,25] This difference could be accounted for by postulating partially overlapping neural populations at the two sides of the cortex, but the same behavior could result solely from interactions at lower levels.

Difference between over-all size of response at the two sides of the cortex is only one factor. Various components of the response at one side have been shown to be affected differently by interaural time and intensity differences.[23,26] Also, various locations on the cortex can be distinguished, some of which are affected primarily by interaural time difference and some primarily by interaural intensity difference.[23]

IV. EFFECT OF NEUROLOGICAL MODIFICATION ON LOCALIZATION OF SOUNDS IN SPACE

There are some published data dealing with the effect of neurological modification on the localization of sounds in space. Included are studies involving ablation of cortical areas and transection of neural pathways in animals[27-31] and studies of pathological conditions in humans.[32,33] Studies of this nature, both in humans and in animals, are necessarily unclear: It is difficult to establish the exact extent of the lesion, the changes in behavior can be subtle, and the exact nature of the stimulus can be critical.

Neural deprivation studies involving localization of sounds in space were reviewed recently by Rosenzweig.[34] Pavlov[31] reported that dogs could not learn a right-left discrimination after the corpus callosum had been sectioned. Girden[27] reported that dogs could retain a learned right-left discrimination after the corpus callosum had been sectioned.

Although it appears that the significant difference between these two observations is the distinction between learning a new discrimination and retaining a previously learned discrimination, we should realize that differences in the stimulus or in the behavioral task might be responsible. It appears that in some sense localization of brief, impulsive stimuli is a more demanding task than localization of stimuli lasting several seconds.[34]

This ambiguity is illustrated by the apparently conflicting results of ten Cate[35] and Neff.[29,30] Ten Cate reported that decorticate cats could orient to an acoustic stimulus. Neff, on the other hand, reported almost complete loss of localization ability in decorticate cats. Neff used impulsive stimuli, while ten Cate used stimuli lasting 10-15 seconds. Again, the difference in stimulus may not be the only difference between the two experiments. Neff reported that the behavioral deficit depended strongly on the extent of the lesion.

In more recent studies, Neff has investigated the effect of unilateral cortical lesions.[29] Although bilateral ablation almost completely destroys ability to localize, little, if any, deficit is observed after unilateral ablation. Unilateral transection of the brachium of the inferior colliculus, on the other hand, produces deficits more pronounced than with even the largest unilateral cortical ablation.

There seems to be only one study involving transection of the main commissural pathways at the subcortical level. This was reported in 1958 by G. Colston Nauman of Neff's laboratory. The corpus callosum, the commissure of the inferior colliculus, and the trapezoid body were transected, singly or in combination. Again we find the results of different studies in conflict. Miss Nauman found, in apparent contradiction of Pavlov's results, little or no change in the cat's ability to localize sounds in space after transection of the corpus callosum, the commissure of the inferior colliculus, or both.[28]

Although Miss Nauman was never completely successful in transecting the trapezoid

body, she did find that even partial transections produced a decrement in the cat's ability to localize sounds in space. She concluded from this fact that the trapezoid body is important for sound localization. Neff makes the following comment[36]:

> From the results of Nauman's study, it may be concluded that for accurate localization of sound in space it is essential that the nerve impulses from the two ears interact at some center in the lower brain stem. When results of anatomical and electrophysiological studies are considered (Stotler, 1953; Galambos, Schwartzkopff, and Rupert, 1959), the medial superior olivary nucleus appears to be the critical center.

Observations from clinical studies are quite restricted. In these studies the emphasis is on behavioral response as a tool for determining the extent of brain damage, rather than on the behavioral response in itself.

Sanchez-Longo and Forster[32] investigated the ability of patients with unilateral temporal lobe lesions to localize sounds in space. Their purpose was to aid in diagnosis of brain damage. They found that the patients are impaired in their ability to localize sounds in the half-field that is contralateral to the lesion.

Another study gives conflicting results. Walsh[33] found that localization on the horizontal plane was not affected by temporal lobe lesions, although localization on the vertical plane was. Again, this conflict may result from differences in the stimulus, differences in the behavioral response or differences in the extent of the lesions.

V. PSYCHOPHYSICS OF BINAURAL LOCALIZATION – EXISTING MODELS FOR THE BINAURAL FUSION PROCESS

The psychophysics of binaural localization and existing models for the binaural fusion process are best treated together. Model building has been based almost exclusively on psychophysical observations, and the extensive published data on psychophysics may assume some degree of coherence if they are treated in connection with the pertinent models.

There is a large body of published data dealing with the psychophysics of binaural phenomena in organisms including man. We shall omit discussion of studies dealing with binaural aspects of signal detection. Of the remaining studies, those dealing with binaural localization of sounds in space, we shall consider only a small sample.

5.1 GENERAL DESCRIPTION OF THE PROCESS OF BINAURAL LOCALIZATION

The normal human listener is capable of determining with a high degree of precision the location of a sound source. Although such factors as intensity, frequency content, and difference of frequency content at the two ears play a role in this process, the two overriding factors for a large class of stimuli are interaural intensity difference and interaural time difference. A sound originating off the median plane reaches the ipsilateral ear first because of the greater distance to the contralateral ear. The sound is more intense at the ipsilateral ear, both because of the inverse square law and because of shadowing by the head.

For tonal stimuli, interaural time (equivalently, phase) difference is the more influential factor at low frequencies, while interaural intensity difference predominates at high frequencies.[37-39] For complex stimuli, the situation is more involved. The localization process utilizes time differences not only of the microstructure of the stimulus but also of the envelope of the stimulus.[40,41]

This is reasonable in terms of results of experiments relating the stimulus to the evoked response at the periphery. The auditory nerve fires synchronously in response to low-frequency pure tones, less so in response to high frequencies; thus we would expect that time would be less influential at high frequencies than at low. Conversely, the shadowing effect of the head is greater at high frequencies than it is at low frequencies; thus we would expect that interaural intensity difference would be more important at high frequencies. The auditory nerve has been shown to fire synchronously to the onset of high-frequency tone or noise bursts,[42] and thus we would expect time differences of the envelope of complex stimuli to be important.

A few representative numbers will illustrate the remarkable precision of the process of binaural localization. The just-noticeable difference for azimuth for pure tones is a function both of the azimuth and of the frequency of the tone. In general, it increases with azimuth and reaches maxima at approximately 2 kc and 8 kc. Under the most favorable conditions (frequency of 500 cps, source located straight ahead), it is approximately

one degree.[43] The influence of interaural time difference and interaural intensity difference can be observed independently if the stimulus is delivered through earphones. The just-noticeable change in interaural intensity difference for tone pulses depends strongly on the frequency of the stimulus and on the absolute intensity of the stimulus. In general, it increases with over-all level. For tone pulses approximately 50 db above threshold, it reaches a maximum of approximately 1 db at 1 kc, and decreases to approximately 0.5 db at higher and lower frequencies.[44] The just-noticeable change in interaural time difference depends on the nature of the stimulus – impulsive or continuous, single or multiple presentation. For low-frequency random noise, it is approximately 5 or 10 μsec.[45]

These numbers are for human observers. The limited evidence that is available indicates that cats are capable of comparable performance. Katz[46] describes experiments in which cats were able to distinguish sources 0.5 meter apart at a distance of 18 meters; these conditions produce an interaural time difference of 2.8 μsec. Miss Nauman[28] gives a value of approximately 10 μsec, again based on free-field experiments.

If the stimulus is delivered through an external source, the listener receives the impression of something "out there." If, on the other hand, the stimulus is delivered through earphones, the effect is quite different. The listener receives the impression of a "virtual source" located inside his head. These two conditions are commonly referred to as "localization" and "lateralization," respectively.

There is reason to believe that the localization and lateralization processes are two aspects of the same phenomenon,[47] with a difference introduced in part by the effect of head movement and in part by other factors, as mentioned in Section I. If head movements are prevented, the interaural time difference resulting from a source located directly in front of the listener is the same as that resulting from a source located directly behind him. For both cases, the stimulus reaches the two ears simultaneously.

Suppose now that the listener turns his head to the right. If the source is located in front, the stimulus will now reach his left ear first; if the source is located behind him, it will reach his right ear first. The listener now has the necessary information to distinguish between the two cases. Similarly, a source directly overhead could be distinguished from a source directly below by tipping the head.

The situation in which the stimulus is delivered through earphones appears to be a special case of the situation described above. Suppose that the stimulus is delivered simultaneously to the two sides. The listener turns his head, but the stimulus still reaches the two ears at the same time. The only possible source location that could produce this effect is actually inside the head, and this is what the listener reports that he hears.

While this discussion is restricted to sources on the median plane, it can be generalized to sources at any location. In general, a given interaural time difference can result from a source located anywhere on a cone-shaped surface. Its azimuth and elevation can then be specified uniquely from the change in interaural time difference

introduced by head movement.

This explanation of the difference between lateralization and localization receives support from an interesting experiment reported by Wallach.[48] He delivered a stimulus through an array of loud-speakers. The loud-speakers were switched by the listener's head movements in such a way that changes in interaural intensity produced by a single source at some prescribed location could be produced synthetically. With this arrangement, it was possible to produce a virtual source "behind" the listener with all of the loud-speakers actually in front. The illusion was not always completely successful; Wallach ascribed this fact to the role of the pinna.

In lateralization experiments, the location of the virtual source is a function of both interaural time difference and interaural intensity difference. If the stimulus reaches the two ears simultaneously, the virtual source will move toward the more intense side. If the stimulus is of the same intensity at the two ears, the virtual source will move toward the side that receives the earlier stimulation. There is some indication (Mickunas,[49] but see also Teas[50]) that the degree of lateralization of the virtual source produced by a given interaural time difference is independent of the absolute intensity of the stimulus.

These two factors can be traded one for the other.[51-53] Over a limited range, an image that has been displaced to one side by making the stimulus at that side more intense, for example, can be restored to the midline by making the stimulus at the opposite side arrive earlier. The mechanism responsible for this trading relationship has been the source of much conjecture. We shall consider the trading relationship more specifically in connection with specific models.

We should note that independent manipulation of interaural time and intensity differences can produce stimulus situations that could not result from a single source located in free space. In the "natural" situation, the stimulus both arrives earlier and is more intense at the ear nearer the source. There is evidence[54] that opposition of interaural time and intensity difference cues, as is required in the centering paradigm, results in a spreading out of the virtual source, and that the virtual source is most well defined when the interaural time and intensity differences correspond to those that could result from a single source in free space.

5.2 "CORTICAL" THEORIES OF BINAURAL LOCALIZATION

Theories of binaural localization can be grouped roughly into two classes: those dealing with the cortical phenomena associated with localization, and those dealing with lower level encoding and processing of binaural stimuli. The two types of theories are not incompatible. Although it may be necessary for certain conditions to exist at the cortex for binaural localization to take place, it is likely that these conditions may be established in part through the intermediary of some more peripheral mechanism.

The earliest theories of binaural localization did not involve any consideration of neural mechanisms. It was realized at an early stage that interaural intensity difference

played a role in localization. At first it was thought that binaural localization was simply a derived property of interaural intensity difference.[34] If the stimulus was delivered only to one ear, it was perceived at that side. If the stimulus was delivered to both ears, it was perceived at both sides, but more at the more intense side. The listener heard the sound at both ears, and by "unconscious inference" translated the interaural intensity difference into a judgment of sidedness.

When it came to be realized that interaural time difference was a factor in localization, this view encountered difficulty. It was difficult to see how a listener could "perceive" an interaural time difference of 10 μsec as such and translate it into a judgment of sidedness. This unsatisfactory state of affairs is illustrated by Wilson and Myers[55] as discussed by Ford.[56] Wilson and Myers suggested that interaural intensity difference was the decisive factor, and that interaural time difference was effective only in producing interaural intensity differences through cross-cranial leakage.

More recent theories are influenced by our knowledge of neural mechanisms. Boring[57] postulated two adjacent, overlapping regions in each hemisphere of the cortex. One region is excited by stimulation of one ear, and the other region is excited by stimulation of the other ear. If the two ears are stimulated equally, the two regions in the cortex are excited equally, "... and the modal locus of the cortical excitation is intermediate between the two extreme positions of the mode in right and left lateral localization."[58] Interaural intensity difference serves to move the mode of cortical excitation in the direction of the more intense sound. Boring still regarded the time theory as a special case of the intensity theory, but felt that previous stimulation in some way served to inhibit later stimulation.

Boring's theory is representative of one class of the "cortical" theories, in which the judgment of sidedness results from the locus of excitation on either of the two hemispheres of the cortex. According to another class of theories (see Keidel, Keidel, and Wigand[23] and Bremer[59] for example), the localization process operates on a comparison of the size of response at the two hemispheres of the cortex. According to these theories, interaural intensity difference produces a difference in size of response at the two sides of the cortex. This would occur even in the absence of any neural interaction between the responses to the two ears, since a stimulus presented monaurally evokes a larger response at the contralateral cortex than at the ipsilateral. There must be interaction, however, for interaural time difference to be effective. Bremer puts this interaction at the medial geniculate body, while Keidel puts it much lower, at the level of the trapezoid body.

5.3 VON BÉKÉSY'S "TUNING" MODEL

The distinguishing feature of the two "cortical" models described above is that they are concerned not as much with the processing of the stimulus as with the cortical events associated with localization. The central processing mechanisms that we shall now discuss may be regarded in a sense as performing operations that make possible the

representation of small interaural time and intensity differences at the cortex.

The earliest detailed model for the processing of small interaural time and intensity differences was described by von Békésy in 1930.[60] He suggested a centrally located group of cells that received inputs from both ears. A wave of excitation swept across this group of cells after stimulation of either ear, starting at the side stimulated and traveling at some rate to the opposite side. If a cell received prior excitation from the left ear, it became "tuned" to the left; if it received prior excitation from the right ear, it became "tuned" to the right. The apparent position of the source was then determined by the relative number of cells tuned to each side.

This model was designed to account for the shift in location of the virtual image produced by changes of interaural time difference in lateralization experiments. If the intensity at the two ears is the same, the virtual image shifts toward the side receiving prior stimulation, and the amount of shift is a function of the interaural time difference. For small interaural time differences, the virtual image moves rapidly as interaural time difference is increased. Beyond a certain "break point," however, the change in position of the virtual image with change in interaural time difference becomes less rapid. Von Békésy accounted for this by postulating a higher density of cells in the middle of the cell group than at the edges.

Although this model accounted for changes in position resulting from interaural time difference, the effect of interaural intensity difference introduced complications. Von Békésy felt that interaural intensity difference could not produce change in position of the virtual image through production of time disparities, for two reasons. First, a given interaural intensity difference produced the same degree of lateralization for high-frequency pure tones as it did for clicks, and it did not seem reasonable that time should have the same effect for these two stimuli. (Von Békésy used tone bursts with fast rise times. Possibly his subjects received timing information from the onset transient.) Second, the interaural time difference corresponding to the "break point," beyond which the virtual image moved more slowly with changes in interaural time difference, increased with increasing intensity. To von Békésy this implied a decrease in conduction velocity within the localization center as intensity was increased.

Von Békésy accounted for changes in position of the virtual image resulting from interaural intensity difference by postulating that the excitation wave from either ear did not excite all of the cells that it encountered, but that an increase of intensity of the stimulus brought more cells into action. In this way either an interaural time difference or an interaural intensity difference could result in unequal numbers of cells being tuned to the two sides and produce lateralization of the virtual image.

This model could be used to account for the time-intensity trading relationship. Since either time or intensity difference could tune more cells to one side than to the other, and since all that mattered in a judgment of sidedness was the relative number of cells tuned to the two sides, interaural time differences could be made to offset interaural intensity differences.

There are objections to this model, but it does have much to recommend it. The model requires not only that higher centers be able to determine whether or not a nerve cell in the central comparator has fired, but also that they be able to distinguish two different modes of firing: response to a stimulus delivered to the left ear and response to a stimulus delivered to the right ear. This faculty does not appear likely in the light of what we know about the nature of nerve impulses. Either a nerve cell responds or it does not, and there is no evidence that a cell can respond in two different ways. On the other hand, von Békésy probably made a worthwhile point in refusing to relegate intensity differences to the role of simply modifying time differences. There is still conjecture today as to whether time difference "produces" intensity difference or intensity difference "produces" time difference. Although we know that latency of response is a function of intensity of the stimulus, the fact is that both intensity and time difference affect the judgment of lateralization, and the relationship is not a simple one.

In 1962, van Bergeijk[61] published a modification of von Békésy's model which is of major interest to us, since it is almost identical to the model that we are suggesting as a result of our own experiments. Van Bergeijk split von Békésy's cell group in two, and identified the two groups with the left and right accessory nuclei of the superior olive. Cells in each group received excitatory inputs from the contralateral ear and inhibitory inputs from the ipsilateral ear. Instead of comparing the number of cells "tuned" to one direction with the number of cells "tuned" to the other direction, higher centers now compared the number of cells excited in the left accessory nucleus with the number of cells excited in the right accessory nucleus.

5.4 COINCIDENCE DETECTOR MODELS

A second major class of central processing mechanisms is that proposed by Jeffress[62] and later elaborated upon by Licklider[63] and by David, Guttman, and van Bergeijk.[51] This model is similar to von Békésy's in that it comprises a centrally located group of cells that receive inputs from both ears. A wave of excitation, starting at the side stimulated and traveling at some rate to the opposite side, sweeps across this group of cells after stimulation of either ear. The distinguishing feature of this model is that a cell fires if and only if it receives simultaneous excitation from both sides. The psychophysical judgment of sidedness is then related to the locus of neural activity.

If the stimulus arrives at the two ears simultaneously, and with the same intensity at each side, the left and right excitation waves start sweeping across the cell group simultaneously, and they meet in the middle. If the stimulus to the left ear precedes the stimulus to the right ear, the left excitation wave gets a "head start" and the two waves meet to the side.

The effect of interaural intensity difference is accounted for by postulating that the rate of conduction of nerve impulses, either to the localization center from the periphery or across the localization center, is a function of stimulus intensity. More intense

stimulation results in more rapid conduction of the nerve impulse, and in this way interaural intensity difference is converted into interaural time difference. The fact that latency of evoked response generally decreases with increasing intensity is held to support this view.[64]

This model is satisfactory for explanation of the simple centering experiment, in which interaural intensity difference is made to offset interaural time difference for wideband impulsive stimuli. The model is less satisfactory for more general phenomena, such as lateralization of high-frequency pure tones, lateralization of narrow-band impulsive stimuli, and time-intensity trading at positions off the midline.

The position of the virtual image resulting from stimulation by high-frequency pure tones is a function of interaural intensity difference only. How can lateralization be accounted for in a model that considers interaural time difference only? David, Guttman, and van Bergeijk[51] postulate a statistical modification of the model in which the number of responses impinging on the central time comparator increases with increase of stimulus intensity, thereby resulting in more coincidences on the side corresponding to the location of the more intense tone.

The time-intensity trading relationship is a function of over-all intensity. This can be explained on the basis of an increased rate of change of latency with change of intensity at low over-all intensity. The time-intensity trading relationship is also a function of frequency for narrow-band impulsive stimuli. This can be explained on the basis of frequency-dependent pathways, each with its own time-intensity trading relationship. Harris[65] reported that virtual images resulting from stimulation by highpass and by lowpass stimulation can be moved "through" each other. Again we must invoke the concept of frequency-dependent pathways. None of these phenomena refutes the model, but we do have the unsatisfactory situation in which each new phenomenon necessitates new assumptions about the model.

A major substantive objection to the coincidence detector comes from an experiment reported by Moushegian and Jeffress.[66] They presented a tone with fixed interaural time and intensity differences, and required the listener to match the position of the resulting virtual image by adjusting the interaural time difference of noise. The noise and tone were presented alternately. With this arrangement, the time-intensity trading relationship for positions off the midline could be investigated. Moushegian and Jeffress found that a given interaural time difference could not be equated simply to a particular interaural intensity difference, but that time had relatively less effect when interaural time and intensity differences were acting in opposition than when they were acting in concert. They concluded that Jeffress' 1948 model must be modified to incorporate inhibition, as well as facilitation. Once again the model must be modified to accommodate new data. This time the modification seems to be such that it changes the very nature of the model.

5.5 CHERRY'S BINAURAL FUSION MECHANISM

One final central processing mechanism should be mentioned. This is the cross-correlation scheme proposed by Cherry and his associates.[40,67,68] This model describes not a possible neural mechanism but rather a possible mathematical operation.

Cherry bases his model on the following psychophysical experiment: Stimuli are delivered through earphones to the two ears of a subject. "The two signals are, respectively, pure and distorted versions of the same signal (perhaps speech). The delay τ [interaural time delay] is randomly set and the listener answers right or left, as the source of sound appears to him to lie. The 'correlation function' then corresponds to the probability distribution of his correct judgments. Such functions represent the degree of aural fusion, and show up strikingly the invariants of speech signals which are significant in aural perception."[69]

According to Cherry's conceptual scheme, the lateralization judgment is effected through a running crosscorrelation of the signals at the two ears. "The two aural signals undergo cross correlation . . . . The resultant function $R_{12}(\tau)$ can be considered, for convenience, as established on a 'conceptual' surface on the model, divided centrally at $\tau = 0$ into a left-half and a right-half region. As the interaural time delays are altered, first positive and then negative, the major peak of the correlation function under discussion would move laterally first to one side then the other, of the central dividing line. Such a model of the fusion mechanism offers a simple framework in which the second process, a judgment mechanism, could operate to assess the left : right dichotomy in position (and, of course, the extent of the perceived displacement from center) of the fused sound image."[70]

This engineering model has some value. Possibly the fusion process can be described by some such operation. Cherry's correlation detector does have much in common with the coincidence detector as described by Licklider.[63] One objection to Cherry's work is that his experimental paradigm does not allow for differentiation between degree of lateralization and definition of the virtual image. A judgment of "virtual source to the left" in 50 per cent of the trials could result, for example, either from a clearly defined virtual source located at the midline or from a completely amorphous virtual source located equally to the right and to the left. Our major objection to this "black-box" model is that it does not permit us to design specific physiological experiments.

VI. METHODS

6.1 EXPERIMENTAL PROCEDURE

We used adult cats weighing 2-4 kg. Cats were rejected if either ear appeared abnormal by external visual inspection or if threshold for either ear was not good. Dial anesthetic (CIBA) was administered intraperitoneally, 0.75 cc per kilogram of body weight. This initial dose was in most cases all that was required. In the few cases in which the animal did get light enough to exhibit a leg-withdrawal reflex, additional doses of 0.2 cc Dial were administered at intervals of approximately 20 minutes. It was necessary to keep the animal at this depth of anesthesia in order to avoid undue pulsation of the exposed portion of the medulla.

Body temperature, as measured by a rectal thermometer, was maintained between 36°C and 38°C. If the temperature went beyond these limits, the experiment was arrested until it could be restored. 50 cc of 0.9 g/100 cc saline solution was administered subcutaneously at 3-hour intervals.

After the anesthetized animal was placed in the headholder, a tracheotomy was performed and a stainless-steel cannula was inserted in the trachea. In order to avoid interference by the cannula with electrode placement, it was found advantageous to put the cannula as far caudal as possible.

An incision was made through the skin along the midline of the head, reaching approximately from the nuchal ridge to the inion node. After the flaps of skin on each side were reflected, the external auditory meatus on each side was exposed and transected to receive the tube through which the auditory stimuli were presented.

The animal was then turned on its back and supported by a V-shaped table built for the purpose. We used the ventral approach to the medulla, similar to that described by others.[2,7] An opening was made by blunt dissection lateral to the trachea, thereby exposing the base of the skull between the left and right auditory bullas. It was then possible to expose the trapezoid body by making an opening through the skull approximately between the most prominent part of the bullas. The dura mater was folded back over the extent of the opening in the skull, and the pia mater was removed under a microscope from the region through which the electrode was to be inserted.

6.2 ELECTRODES

After a great deal of experimentation with various types of electrodes, we settled on a stainless-steel microelectrode with a platinum-black tip. This electrode was relatively easy to make, and we found its recording properties to be satisfactory for our purposes. Also, with this electrode it was possible to mark the electrode recording position, as described in section 6.4. A major disadvantage of this electrode was that it was very fragile; it was necessary to remove the pia mater surgically to prevent the electrode tip from being broken off.

The etching and insulating of the electrode were identical to that described by Brown

and Tasaki[71]: Size 00 stainless-steel insect pins were etched electrically in a solution made by mixing one part concentrated hydrochloric acid with one part 3-molar potassium chloride solution. Some of the potassium chloride precipitated out of solution when the acid and salt solutions were mixed, and a saturated solution suitable for etching remained.

In the etching procedure, a carbon block served as reference electrode. The steel pin was dipped rapidly in and out of the etching solution with a voltage of approximately 3 volts rms, 60 cps, applied between the pin and carbon block. This process was continued until enough steel was removed so that the pin was a few millimeters shorter than its original length. The voltage was then reduced to approximately 1 volt rms, and the pin was dipped rapidly in and out of the etching solution another 20 or 30 times. Objectionable splattering was prevented by means of a layer of xylene floating on top of the etching solution. Immediately after the low-voltage etching, the electrode was dipped successively into concentrated (but not saturated) sodium carbonate solution, 5 per cent acetic acid solution, ethyl alcohol, and xylene. The end result was an electrode with a tip diameter of less than 1 μ and a taper of 10-15 μ per 100 μ of length. The entire process could be carried out quickly without the aid of a microscope, and the yield rate was of the order of 80 or 90 per cent.

The electrode was insulated with Insl-X (E-33 clear). The Insl-X was thickened until it was approximately the consistency of honey. The electrode was dipped into the Insl-X point down, then withdrawn rapidly. A drop of Insl-X formed over the point of the electrode. After approximately 5 seconds, the electrode was turned point up. The Insl-X flowed back over the shaft, but the pellicle remained, insulating all but the tip. If the Insl-X was too thin, the drop fell off the tip. If it was too thick, it would not flow back over the shaft satisfactorily. The electrode was left tip up, at room temperature, to dry overnight. This insulating procedure also could be carried out quickly, without the aid of a microscope. We were unable to achieve yield rates higher than approximately 50 per cent.

The procedure for plating a tip on the electrode has not been described by other authors. Since platinum black will not adhere satisfactorily to stainless steel, we found it necessary to apply an intermediate layer of copper. The insulated electrode was placed in a copper cyanide plating solution with a reference electrode of oxygen-free copper. A 1.5-volt battery in series with a 5- or 10-megohm resistor was placed between the steel electrode and the copper, with the steel electrode negative. In approximately 20 seconds enough copper was deposited on the uninsulated tip to form a ball 2-3 μ in diameter (see Fig. 4). This procedure was carried out best under a microscope. The electrode was removed from the plating solution and rinsed in distilled water. The electrode was then placed in a plating solution of 1 per cent platinum chloride, 5 per cent agar,[73] with platinum wire as the reference electrode. A 1.5-volt battery in series with a 5- or 10-megohm resistor was placed between the steel and platinum for another 15-20 seconds, or until the ball on the tip of the electrode measured 3-5 μ in diameter

(see Fig. 4). The electrode was rinsed in distilled water and stored until it was used. We obtained the most satisfactory results by using the electrode on the same day that the tip was plated.

The electrode in service was held in a hypodermic needle, which in turn was attached to the plunger of a hypodermic syringe. This syringe was attached to the H-bar of a

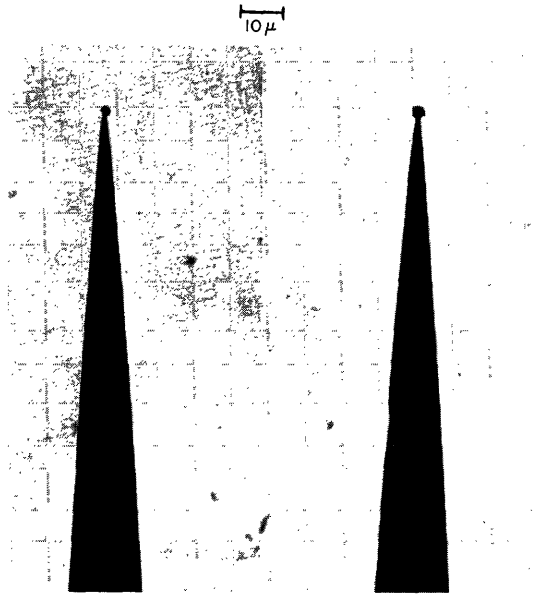


Fig. 4. Two pictures of the same stainless-steel microelectrode. Left: Copper ball plated on tip. Right: Platinum black plated over copper.

stereotaxic instrument, so that the electrode could be positioned over the proper area of the medulla. The fact that we used insect pins as blanks for the electrodes provided a most satisfactory method of fastening the electrode to the hypodermic needle. If the blunt end of the insect pin was etched, the other end could be pushed into a 26G hypodermic needle. The resulting force fit held the electrode in place securely, with good electrical contact between the electrode and hypodermic needle.

The hypodermic syringe was connected by approximately 20 feet of 0.125 in. O.D. nylon pressure tubing to a second syringe outside the chamber. The two syringes and connecting tubing were filled with mineral oil that had previously been boiled under vacuum to eliminate air and moisture. The syringe outside the chamber was attached to a micrometer, with the result that the depth of penetration of the electrode could be controlled from outside the chamber.

6.3 STIMULUS GENERATION

Acoustic clicks were generated by applying rectangular voltage pulses of 100-μsec duration to a matched pair of Permoflux PDR-10 earphones. The earphones were enclosed in brass housings, and plastic tubes, 2.5 inches long, led the stimulus from the earphones to the external auditory meatus of the cat. In this way each earphone was closely coupled to the eardrum of the corresponding side, and the possibility of acoustic

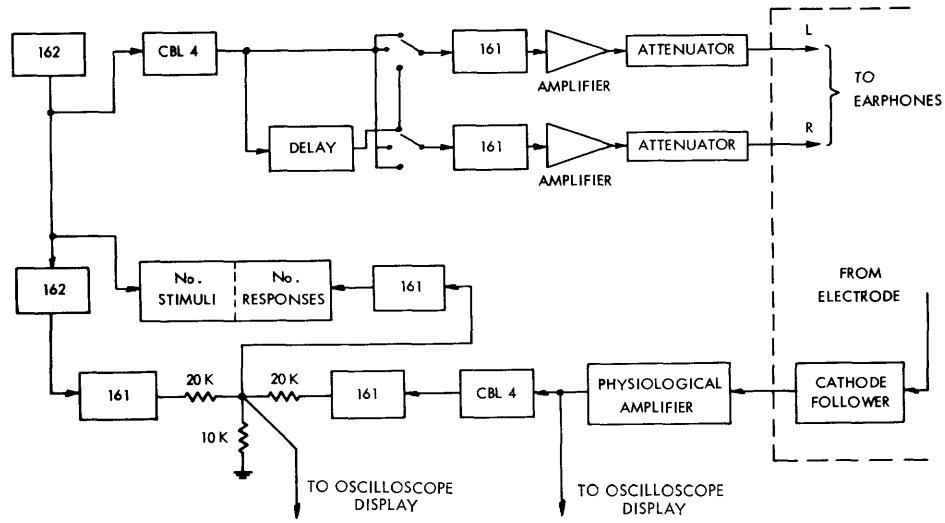


Fig. 5. Block diagram of equipment arrangement. Numbers 161 and 162 refer to Tektronix Pulse and Waveform Generators, respectively.

leakage from one side to the other was minimized. The cat was isolated in a soundproof, electrically shielded chamber.

The stimulus generation is shown schematically in Fig. 5. A Tektronix 162 Waveform Generator put out pulses at the rate of approximately three per second. These pulses went to a CBL4 Schmitt trigger unit,[74] through a calibrated adjustable delay unit, to a two-pole three-throw switch. The three positions of this switch corresponded to left leading, simultaneous, and right leading. The synchronization pulses from the switch were led to a pair of Tektronix 161 Pulse Generators, each of which put out rectangular voltage pulses of 100-μsec duration. The pulses from the Tektronix 161 Pulse Generators excited MacIntosh 20-watt power amplifiers. The amplified pulses were fed through output attenuators to the earphones. At a reference level of 0 db, the voltage across the input terminals to an earphone was 4 volts, which corresponds to a peak output pressure into a rigid 1-cc coupler of approximately 135 db with reference to 0.0002 dyne/cm^2.[75]

The arrangement for processing the spike responses is shown in the bottom part of Fig. 5. Electrical activity from the electrode was fed into a cathode follower, then out of the chamber to an Offner Model 142 high-gain amplifier, at which point it was monitored on an oscilloscope. We wished to count the number of stimulus presentations to which a nerve cell responded. Since the action potential from the nerve cell was in general no larger than the slow-wave activity, it was necessary to use a gating procedure. The output from the Offner amplifier was fed to a CBL4 Schmitt trigger. This Schmitt trigger was adjusted to put out pulses when there was an action potential. When adjusted to this level, the Schmitt trigger would generally also be triggered by the slow-wave potential. Synchronization pulses from the Schmitt trigger went to a Tektronix 161 Pulse

Generator that put out 50-volt, 500-μsec pulses. These pulses went into one side of a resistive adder. Into the other side of the resistive adder were fed 50-volt pulses (we shall call them gating pedestals) from another Tektronix Pulse Generator. The onset time and duration of these gating pedestals could be adjusted to span the interval over which spike responses occurred, but to exclude the interval corresponding to the slow-wave potential. A mechanical counter could then be made to count when and only when the 500-μsec pulses occurred during the longer gating pedestal. In order to avoid multiple counting if the cell responded more than once to a single stimulus presentation, a third 161 Pulse Generator was put at the output of the resistive adder, adjusted to put out a pulse longer than the gating pedestal. These pulses were counted. A photograph of a typical oscilloscope trace is shown in Fig. 6. The top trace is the output of the physiological amplifier, and the bottom trace is the output of the resistive adder. Although the output of the physiological amplifier crosses the trigger level for the Schmitt trigger three times, only the crossing corresponding to the spike response occurs simultaneously with the gating pedestal. The number of stimulus presentations was also counted.

6.4 HISTOLOGICAL CONTROLS

As mentioned in section 6.2, it was possible to mark the position of stainless-steel electrodes in the brain. We used essentially the same procedure as that described by Brown and Tasaki.[71] Iron from the electrode tip was deposited in the brain by passing a small current from the electrode to the brain (electrode positive). We used a current of 3 μa, produced by a 300-volt battery in series with a 100-megohm resistor, for 15 seconds. A microammeter in series with the electrode verified that the proper current was passing through the electrode, and the electrodes were inspected under a microscope to determine that the iron went out through the electrode tip and not through any break in the insulation along the electrode shaft.

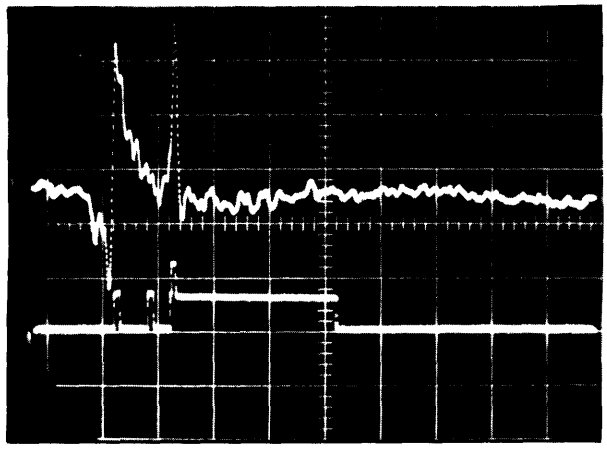


Fig. 6. Typical oscilloscope trace. Top, output of physiological amplifier. Bottom, output of resistive adder. Scale, 2 msec/division.

The cat was perfused with formalin containing 3 per cent ferrocyanide and 3 per cent ferricyanide. This procedure, according to Brown and Tasaki, binds the iron before it can diffuse.

After fixation, the brain stem was embedded in celloidin, sliced into 20-μ sections, and stained. The iron deposits showed up as patches of Prussian blue. We obtained satisfactory results with cresyl violet stain. Weil stain was not satisfactory, since the blue spots did

not show up sufficiently.

Since this marking procedure destroys the electrode and introduces foreign material into the brain, we did not do histology routinely. A number of cats were set aside for purely histological purposes and a number of marks were made in each. Results are given in section 7.2.

VII. ELECTRICAL ACTIVITY IN THE ACCESSORY NUCLEUS

7.1 PROCEDURE

Our electrode placement was much the same as that used by Galambos et al.[2] The electrode was positioned over the ventral surface of the trapezoid body at an angle of approximately 30° off vertical. The door to the soundproof chamber was shut, the lights turned off, and the electrode was advanced slowly by means of the remote-control hydraulic micromanipulator. As the electrode was advanced, we observed the electrical activity picked up by the microelectrode on an oscilloscope.

We used a "search" stimulus consisting of clicks presented to the two ears at a moderate intensity, usually -50 db re a reference level of 4 volts peak-to-peak across the earphones. (Hereafter, all intensities will be given relative to this reference value. See section 6.3 for acoustic calibration.) These clicks were usually presented with an interaural time difference of 25 msec, the click to the contralateral ear leading. At this delay, we found little interaction between the stimuli to the contralateral and ipsilateral ears. The search stimulus was presented with a repetition period of 320 msec.

As a measure of cell activity we took the relative frequency of firing, defined as the number of stimulus presentations in response to which the cell produced at least one action potential divided by the total number of stimulus presentations. This was measured and plotted for individual cells while the experiment was being carried out. We presented a given number of stimuli, usually 50. As the stimuli were being presented, we observed both the electrical activity of the cell and the output of the resistive adder, as shown in Fig. 6, to determine that we were counting when and only when the cell fired.

When we had completed our observations of a cell, we recorded the depth of penetration of the electrode. We also recorded the electrode depth at which the slow-wave potential reversed polarity in order to determine the position of the cell with respect to the accessory nucleus (see section 7.2).

7.2 SLOW-WAVE POTENTIAL

As the electrode was advanced, we saw two distinct kinds of electrical activity. One was what Galambos et al.[2] termed a "slow-wave" potential; the other was action potentials from individual cells.

The slow-wave potential follows in detail the pattern described by Galambos. Ventromedial to the accessory nucleus, stimulation of the contralateral ear evokes a negative-going slow-wave potential, and stimulation of the ipsilateral ear evokes a positive-going slow-wave potential. As the electrode passes through the accessory nucleus, these potentials reverse, so that dorsolateral to the accessory nucleus stimulation of the contralateral ear evokes a positive-going potential and stimulation of the ipsilateral ear evokes a negative-going potential.

This "slow-wave" potential is slow in name only. The initial excursion, in particular, is as steep as excursions occurring in the action potentials from individual cells. It does,

however, have characteristics associated with graded potentials. The response changes gradually with changes in stimulus intensity and electrode location, and it is not all-or-none.

We did not study the slow-wave potential in detail, since our main interest was in binaural interactions in individual nerve cells. Preliminary observations indicate that, regardless of electrode position, there is little or no interaction between slow-wave potentials evoked by stimulation of the two ears. The slow-wave potential evoked by stimulation of the two ears appears to be the arithmetic sum of the slow-wave potentials evoked by stimulating the two ears separately. We observed evidence of such linear summation in our early exploratory studies, but we have not pursued this question in detail.

Our main interest in the slow-wave potential was that it provided a measure of the position of the electrode tip with respect to the accessory nucleus. If, as Galambos has stated, the slow-wave potential reverses polarity as the electrode passes through the accessory nucleus, it would provide a convenient way of determining the location of a given cell with respect to the accessory nucleus. In order to verify this, we marked the electrode position at which the slow wave from stimulation of the contralateral ear reversed polarity in a number of cats. Results from one such cat are shown in Fig. 7. Figure 7a, 7b, and 7c shows sections 0.9, 2.1, and 2.5 mm rostral to the caudal border of the trapezoid body. In each of these sections a mark is visible near the ventromedial border of the accessory nucleus. Figure 7d is a section 0.7 mm rostral to the rostral border of the trapezoid body. This is rostral to the accessory nucleus, and we did not observe a slow-wave potential on this pass. These and similar results from other cats led us to conclude that the slow-wave potential does indeed provide a satisfactory measure of position of the electrode tip with respect to the accessory nucleus.

In some passes the slow wave from the ipsilateral ear reversed at a point some distance beyond the reversal point for the slow wave from the contralateral ear. This observation, coupled with subsequent investigation of histological material, is suggestive of the possibility that the slow wave from the contralateral ear may reverse at the ventromedial margin of the accessory nucleus and the slow wave from the ipsilateral ear may reverse at the dorsolateral margin.

7.3 "TIME-INTENSITY TRADING" CELLS

When a cell was isolated, we first measured the relative frequency of firing for monaural clicks, as defined in section 7.1, by presenting 50 clicks at a repetition period of 320 msec and counting the number of stimulus presentations in response to which the cell produced at least one action potential. This procedure was carried out at a number of stimulus intensities for each ear. We then investigated binaural interaction, systematically varying average intensity, interaural intensity difference, and interaural time difference. We presented 50 stimuli for each stimulus configuration and counted the number of stimulus presentations that evoked at least one action potential. Frequent

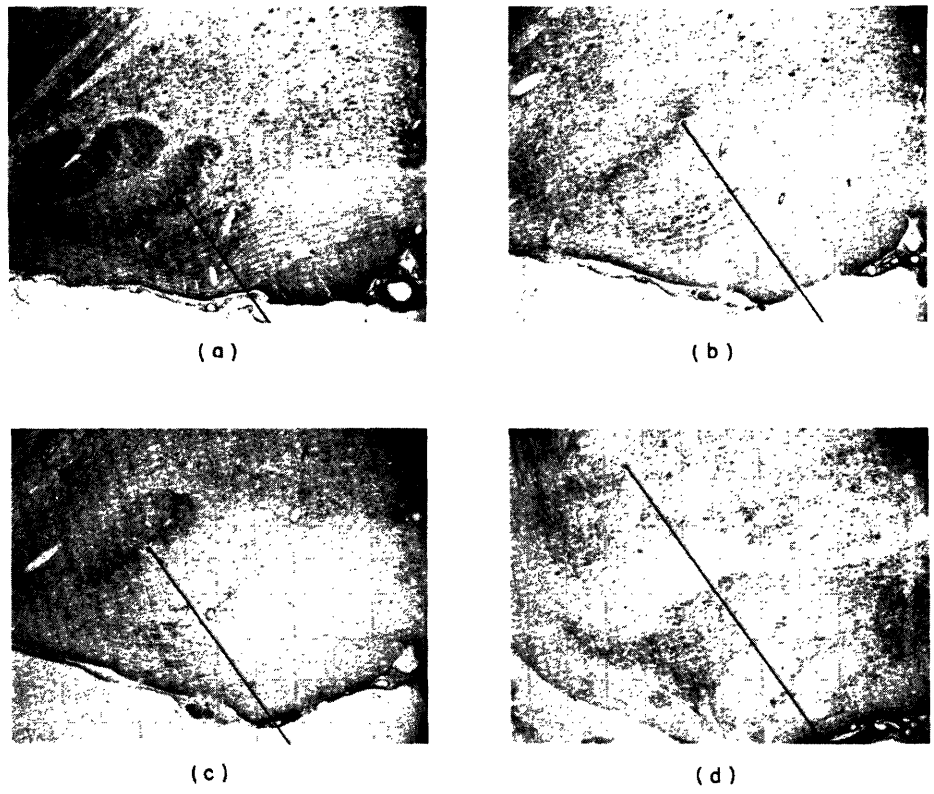


Fig. 7. Histological control of electrode position. Marks were made at the point at which the slow-wave potential resulting from stimulation of the contralateral ear reversed polarity. These marks can be seen more clearly in the original sections as blue spots. We have drawn in lines terminating on the electrode marks in order to give an approximate indication of the electrode tracks. In general, the electrode tracks cannot be seen in the original sections.

checks on the stability of the preparation were made by repeating an earlier stimulus configuration and comparing results.

Results shown in Fig. 8 are from a cell that is representative of the group of cells in which we are most interested. This cell was located in the left accessory nucleus. The abcissa is interaural time difference, $\Delta\tau$, and the ordinate is the relative frequency of firing, based on 50 stimulus presentations. The intensity of the stimulus to the right ear was held constant at −40 db re 4 volts across the earphone, and the intensity of the stimulus to the left ear appears as a parameter.

Cells in this group respond to monaural stimulation of the contralateral ear but not to monaural stimulation of the ipsilateral ear. An interesting feature of these cells is that they are sensitive to both interaural time difference and interaural intensity difference. If the intensity of the stimuli to the two ears is held constant and the stimulus to the ipsilateral ear is made to follow the stimulus to the contralateral ear, then the relative frequency of firing increases. Similarly, if the timing relationships are held constant and the stimulus to the ipsilateral ear is made less intense than the stimulus to the

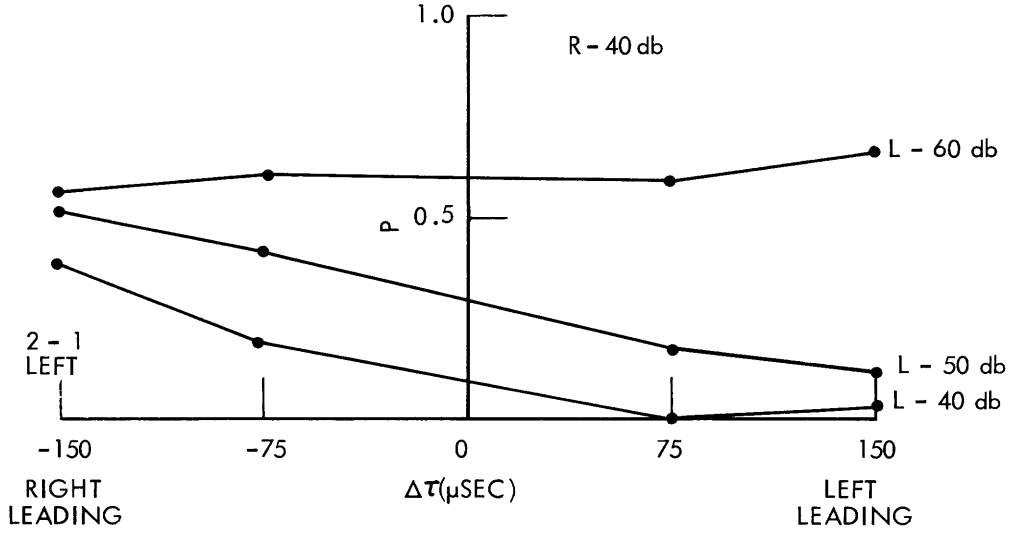


Fig. 8. Effect of interaural time difference and interaural intensity difference on relative frequency of firing P for cell 2-1, located in left accessory nucleus. $\Delta\tau$ is time difference between clicks in left and right ears.

contralateral ear, then the relative frequency of firing increases. These properties can be summarized by saying that the cell is excited by stimulation of the contralateral ear and inhibited by stimulation of the ipsilateral ear, and that the degree of inhibition is a function of interaural time difference and interaural intensity difference.

We were able to obtain data on approximately 60 cells of this type. Every cell was excited only by monaural stimulation of the contralateral ear. Activity of these cells is covered in more detail in Section IX.

Our usual method of recording activity suffered from the shortcoming that it did not provide for measurement of the firing latency of the cells, but gave us only the relative frequency of firing. For a few cells we did record cell activity on magnetic tape and were able to measure firing latency in more detail. Results from one such cell are shown in Fig. 9. Here, the stimulus was presented only to the contralateral ear. As the intensity increased, the relative frequency of firing increased and the average latency decreased. The shift in latency was sharpest near threshold.

The latencies shown in Fig. 9 are average latencies. There was some variability of latency for a given cell with a given stimulus configuration, as shown in Fig. 10. Figure 10 is a dot display of cell firings.[76] For the particular situation in Fig. 10 the stimulus was presented only to the contralateral ear and the intensity was such that the cell responded to almost every stimulus presentation. In general, the variability of the latency increased as the relative frequency of firing decreased and the latency increased.

Although we did not usually record our data on magnetic tape, we did obtain, for all cells that we observed, a rough estimate of average latency at a stimulus intensity

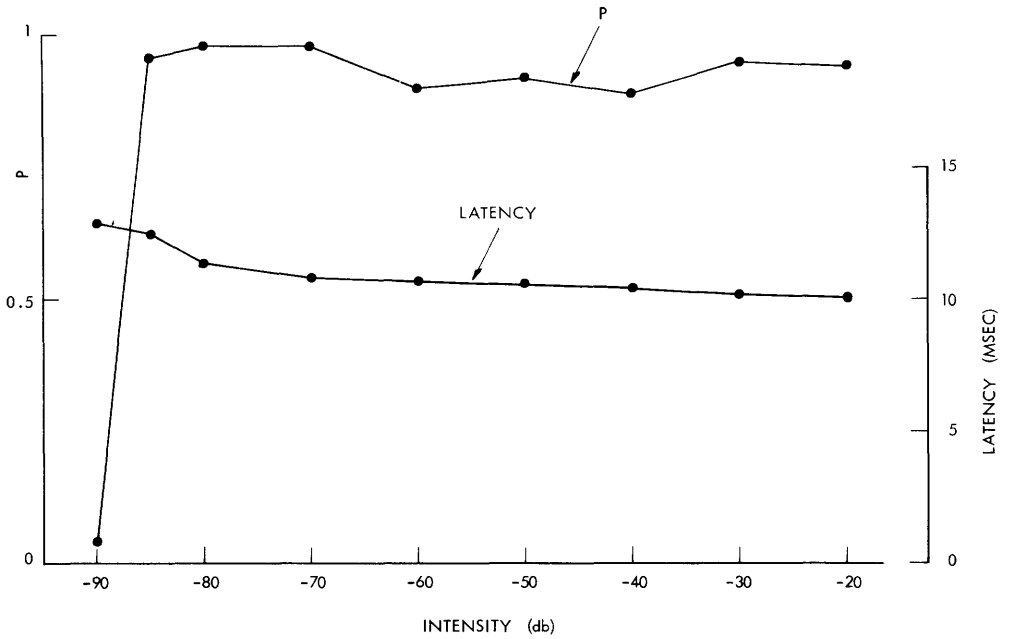


Fig. 9. Effect of intensity on latency and relative frequency of firing P of typical cell. Contralateral stimulation only.

for which the cell responded to almost every stimulus presentation. The average latency was determined by visual inspection of oscilloscope traces. A histogram of the average latencies of 50 cells is given in Fig. 11. It must be understood that these values are approximate.

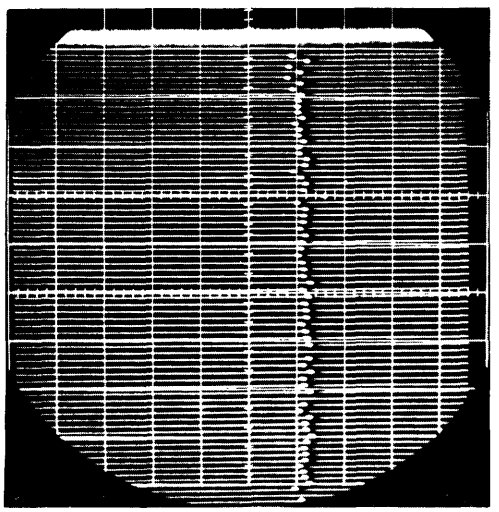


Fig. 10. Dot display of response latencies in successive trials for a typical cell. Each sweep is initiated at the time a stimulus is presented. The bright spot corresponds to the time at which the cell fires. Scale: 2 msec per division.

The cell shown in Fig. 9 is typical of almost all cells that we observed in that it showed a monotonic increase in relative frequency of firing with increasing stimulus intensity. We observed one cell that behaved quite differently. The relative frequency of firing for this cell reached a maximum at −45 db below reference level and decreased at higher intensities, not firing at all at −30 db. The response of this cell was anomalous in one other respect: The role of interaural time difference was reversed. The cell responded more when the stimulus to the ipsilateral ear led than when the stimulus to the contralateral ear led.

The cell shown in Fig. 9 had a

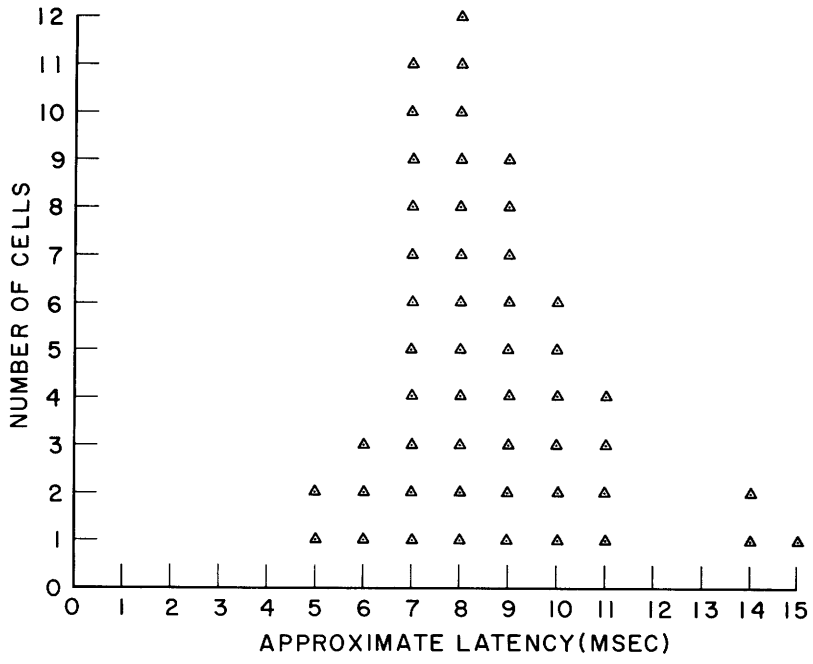


Fig. 11. Histogram of approximate latency of 50 cells. Visual estimate of latency. Stimulus intensity, 20-30 db above threshold for each cell.

relatively sharp threshold, responding rarely at -90 db and responding to almost every presentation of a contralateral click alone at -85 db. One measure of the sharpness of threshold is the change in intensity of the contralateral click required to bring the cell from a relative frequency of firing of 0.2 to a relative frequency of firing of 0.8. Figure 12 is a histogram of this change in intensity for 44 cells. These results are influenced by the fact that we generally changed intensity in steps of 5 db.

Figure 13 shows a histogram of the intensity of the contralateral click presented alone which is required for a relative frequency of firing of 0.5, for 49 cells. Most cells fall in the range from -50 db to -80 db. The lack of cells above -50 db may be due in part to the fact that our search stimulus was usually presented at -50 db.

7.4 OTHER CELLS SHOWING EVIDENCE OF BINAURAL INTERACTION

The cells described in section 7.3 are of special interest to us, since they have properties that are appropriate for inclusion in a neural model for localization of binaural click stimuli. We observed other cells that showed evidence of binaural interaction but could not be grouped with the time-intensity trading cells. We shall describe, in passing, two such groups.

Some cells summed the stimuli to the two ears, in the sense that if stimuli were presented simultaneously to the two ears they responded more than

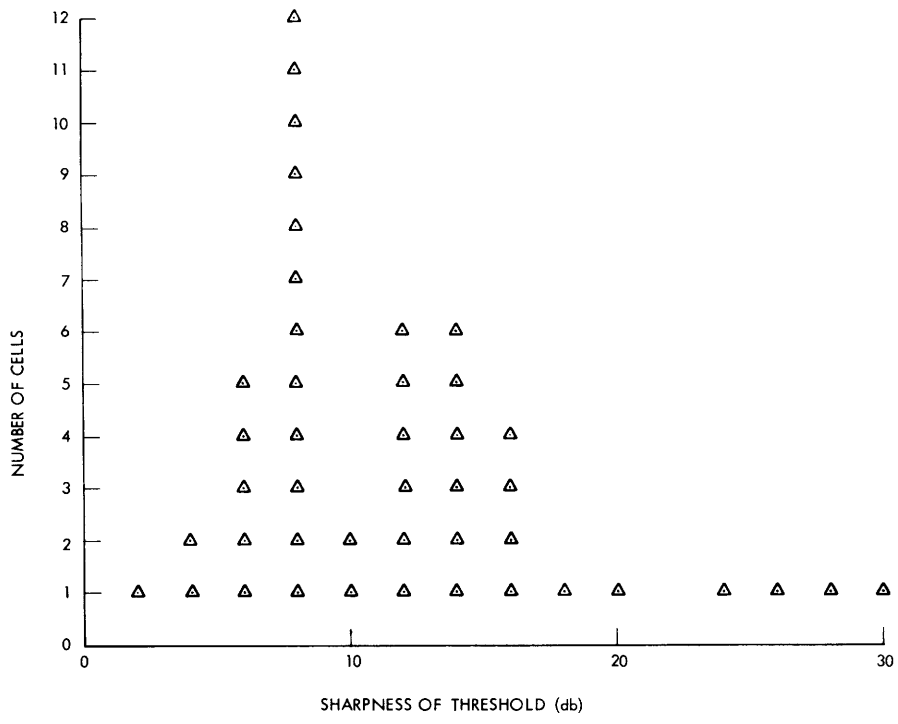


Fig. 12. Histogram of sharpness of threshold of 44 cells. Change in intensity of the contralateral click required to bring cell from relative frequency of firing of 0.2 to relative frequency of firing of 0.8.

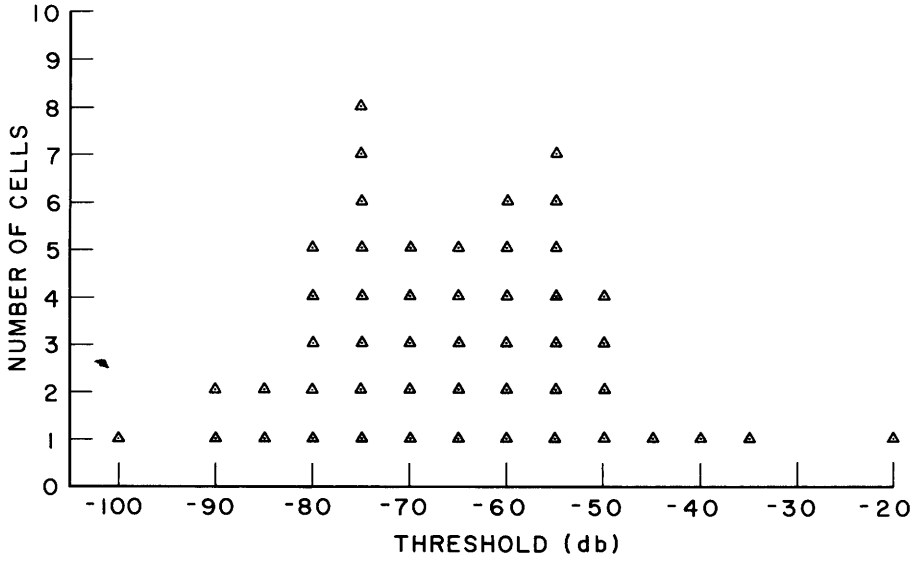


Fig. 13. Histogram of "threshold" of 49 cells. Intensity of the contralateral click required for relative frequency of firing of 0.5.

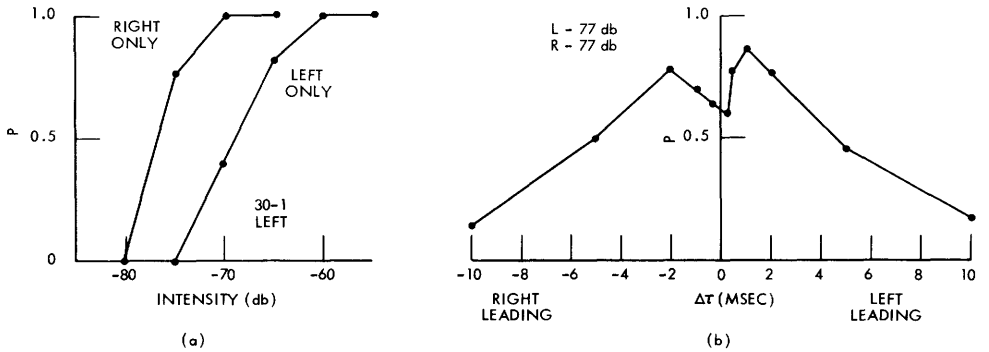


Fig. 14. Cell showing summation of stimuli to two ears. (a) Monaural intensity series. (b) Effect of interaural time difference. Cell on left side.

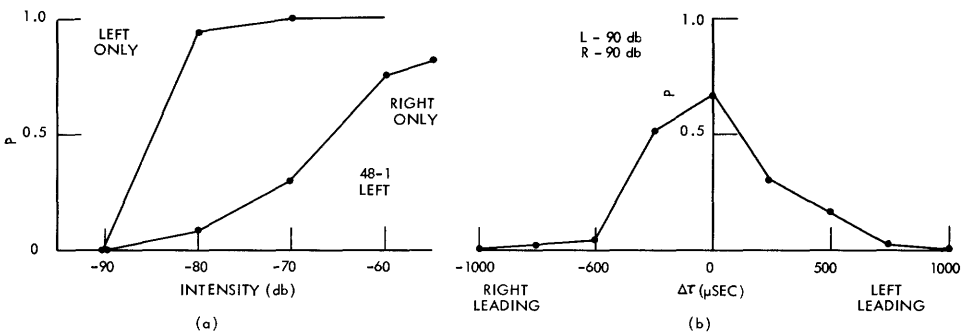


Fig. 15. Cell showing summation of stimuli to two ears. (a) Monaural intensity series. (b) Effect of interaural time difference. Cell on left side.

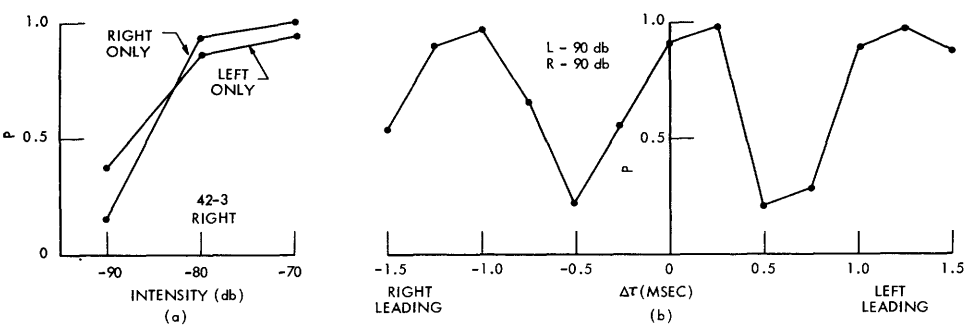


Fig. 16. Cell showing "cyclic" interaction of stimuli to two ears. (a) Monaural intensity series. (b) Effect of interaural time difference. Cell on right side.

they responded to stimulation of either ear alone. This summation extended over several milliseconds, as shown in Fig. 14, or over a few hundred microseconds, as shown in Fig. 15. We observed this property in approximately 20 cells.

Other cells exhibited the "cyclic" behavior shown in Fig. 16. As the interval between the clicks to the two ears was varied, the unit showed several successive peaks of excitability. We saw three such cells, each with a time between adjacent peaks of approximately 1 msec.

VIII. A MODEL FOR THE BINAURAL LOCALIZATION OF CLICKS

We have seen that there are cells in the accessory nucleus of the superior olive which are sensitive to both interaural time difference and interaural intensity difference of binaurally presented clicks. These two parameters are also involved in the psychophysical process of binaural localization of these stimuli. This parallel has led us to suggest a model for the process of binaural localization of clicks based on the activity of time-intensity trading cells. In this section we describe the model and state the assumptions used to obtain parameters of the model from our electrophysiological data. In subsequent sections we investigate the application of the model to specific aspects of binaural localization of click stimuli.

8.1 THE MODEL

The model is illustrated schematically in Fig. 17.[77] We assume that there is a group of cells on the left side of the brain and a symmetrical group of cells on the right side of the brain. We identify these groups of cells with the left and right accessory nuclei. Cells in the left accessory nucleus are excited by stimulation of the right ear and inhibited, in the sense defined in Section VII, by stimulation of the left ear. Cells in the right accessory nucleus are excited by stimulation of the left ear and inhibited by stimulation of the right ear. In keeping with our electrophysiological data, we assume that the cells have a distribution of thresholds. As the stimulus to the right ear, for example, increases in intensity or arrives earlier, more cells are excited in the left accessory nucleus. As the stimulus to the left ear becomes more intense or arrives earlier, fewer cells are excited in the left accessory nucleus. The situation is identical for cells in the right accessory nucleus, with the roles of stimuli to the left and right ears interchanged. Ascending fibers go to higher auditory centers.

The psychophysical judgment of sidedness is based on a comparison of the amount

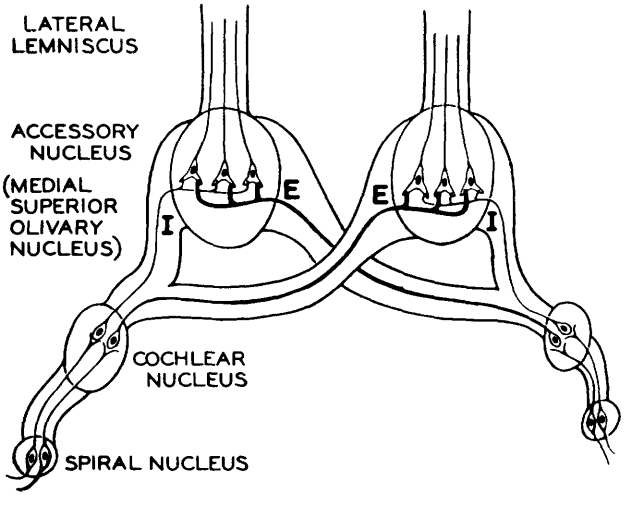


Fig. 17.

Schematic representation of model as given by van Bergeijk.[77] Cells in both left and right accessory nuclei are innervated by excitatory inputs from the contralateral ear and inhibitory inputs from the ipsilateral ear. Ascending fibers from both accessory nuclei go to hypothetical "higher centers." The psychophysical judgment of sidedness is based on a comparison of the amount of response activity at the two accessory nuclei.

of response activity in the left and right accessory nuclei. If the same number of cells responds on the two sides, the virtual image is perceived at the midline. If more cells respond on the left side than on the right, the image is perceived toward the right. If more cells respond on the right side than on the left, the image is perceived toward the left. This crossed representation is dictated by our data and is in keeping with that which is known about neural representation of stimuli in other modalities.

To illustrate the operation of the model, let us investigate the patterns of activity that might result from various combinations of interaural time and intensity difference. Several stimulus conditions are represented in Fig. 18. The numbers of cells responding in the left and right accessory nuclei are indicated by the shaded areas in the two vertical bars. In Fig. 18a, clicks are presented simultaneously to the two ears, with no interaural intensity difference. Since the two sides are equally represented, the same number of cells responds in the left and right accessory nuclei and the source is perceived at the midline.

In Fig. 18b, the stimuli to the two ears are of equal intensity, but the stimulus to the left ear precedes the stimulus to the right ear. The stimulus arriving first is excitatory for cells in the right accessory nucleus and inhibitory for cells in the left accessory nucleus, so that more cells respond on the right than on the left, and the virtual image is perceived toward the left.

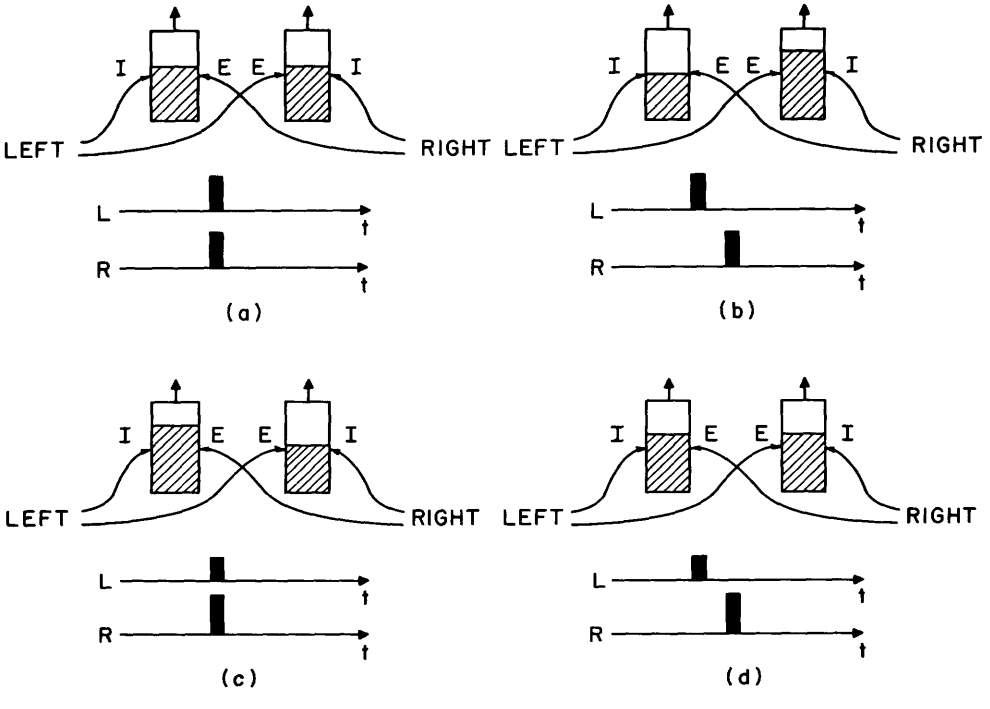


Fig. 18. Operation of the model. The shaded area represents the number of cells responding to a stimulus presentation. (a) $\Delta\tau = 0$, $\Delta I = 0$. (b) $\Delta\tau \neq 0$, $\Delta I = 0$. (c) $\Delta\tau = 0$, $\Delta I \neq 0$. (d) $\Delta\tau \neq 0$, $\Delta I \neq 0$.

Figure 18c illustrates the condition of simultaneous stimulation with an interaural intensity difference. The stimulus to the right ear is more intense than that to the left, so that more cells respond in the left accessory nucleus than in the right. The virtual image is perceived toward the right.

In Fig. 18d, the stimulus to the left ear is less intense than the stimulus to the right ear, but it arrives earlier. Although it is impossible at this point to make any statement about the relative contributions of interaural time difference and interaural intensity difference, in terms of the model there would be combinations of time and intensity differences which would result in equal activity in the left and right accessory nuclei. For appropriate configurations, the interaural time difference would offset the interaural intensity difference and the same number of cells would respond at the two sides.

This model is identical to one proposed by van Bergeijk.[61] As pointed out by van Bergeijk, it is conceptually equivalent to a model suggested in 1930 by von Békésy.[60] The value of this model is that it provides a physiologically reasonable mechanism for binaural localization of sounds. It could in some sense be regarded as a "transducer," converting differences of interaural time and intensity into differences of the number of cells excited in the left and right accessory nuclei.

8.2 RELATION OF ELECTROPHYSIOLOGICAL DATA TO THE MODEL

The model described above operates on a comparison of the number of cells in the left and right accessory nuclei firing in response to a single stimulus presentation. Our raw data appear in a quite different form. We actually observed the number of times that an individual cell fired in response to a given number of stimulus presentations. In order to relate these data to the operation of the model, we must make a number of assumptions.

Our first assumption is that an individual nerve cell fires in response to a stimulus presentation with probability P, and remains quiescent with probability (1-P), where P is estimated to be equal to the experimentally determined relative frequency of firing (see Appendix A). Throughout the balance of this report we shall use P to denote either the empirical relative frequency of firing of a real nerve cell or the probability of firing of a cell in the model, its use depending on the context.

We assume also that each cell that we observe is representative of a population of cells. We assume that if we observe an individual cell with certain properties, there is actually a large number of cells in the accessory nucleus with similar properties. We have an estimate of the time-average probability of firing, based on the relative frequency of firing. We assume that this is equal to the ensemble-average probability of firing for the cells in the population.

We assume that firings of individual cells within a population are statistically independent. This assumption is certainly not strictly justified, because of possible systematic fluctuations in excitability. It probably does represent a reasonable approximation. A most compelling justification of this assumption is that we have no

rationale for making any other.

These assumptions make it possible to obtain an estimate of the proportion of cells in a population responding to a single stimulus presentation, given the relative frequency of firing of a single cell. If the relative frequency of firing of a single cell is equal to P, then P is also our estimate of the ensemble-average probability of firing for all cells in the population. If there are n cells in the population, then on the average a number nP of these cells will fire in response to a single stimulus presentation.

We next assume that the system is symmetrical. That is, we assume that each cell that we observe is representative not only of a population of cells on the same side, but also of a population of cells in the accessory nucleus on the opposite side, with the only difference being that the roles of "left" and "right" are reversed. This assumption is necessary in order to be able to make any statement about the number of cells responding at the two sides.

As a specific example, consider the cell of Fig. 19a. This cell was located in the right accessory nucleus. We first measured relative frequency of firing for interaural time differences ranging from right leading by 500 μsec to left leading by 500 μsec, with the intensity at the left ear -60 db and the intensity at the right ear -65 db. In order to obtain the relative frequency of firing of the hypothetical symmetrical cell in the left accessory nucleus under the same stimulus conditions, we then measured relative frequency of firing for interaural time differences ranging from right leading by 500 μsec to left leading by 500 μsec, with the intensity at the right ear -60 db and the intensity at the left ear -65 db. According to our assumption of symmetry, the only difference between the hypothetical cell and the cell actually observed is that the roles of "left" and "right" are interchanged, so that the activity of the hypothetical cell is obtained by interchanging "left" and "right," both for intensity and for interaural time difference, for the second curve. The resulting activity of the two cells, now for the single intensity condition left -60 db, right -65 db, is shown in Fig. 19b.

Some of the cells actually observed were on the right, some on the left. In keeping with the assumption of symmetry, we shall henceforth avoid the terms "left" and "right," and use instead the terms "ipsilateral" and "contralateral," where these terms are understood to refer to electrode placement. Wherever we refer to the activity of two cells in the two accessory nuclei, only one of these cells, the one on the ipsilateral side, was actually observed. The other one, on the contralateral side, is a hypothetical symmetrical cell.

We need a measure of relative activity in the accessory nuclei at the two sides. To keep the present discussion simple, we first assume that one cell that we studied is representative of all cells in the accessory olivary nuclei. Later this assumption will be modified, when we base the model on data from many cells.

For a given stimulus configuration, we obtain from our experimental data two key parameters of the model, P_I and P_C. These are the probabilities of cell firings in the populations of cells in the ipsilateral and contralateral accessory nuclei, respectively,

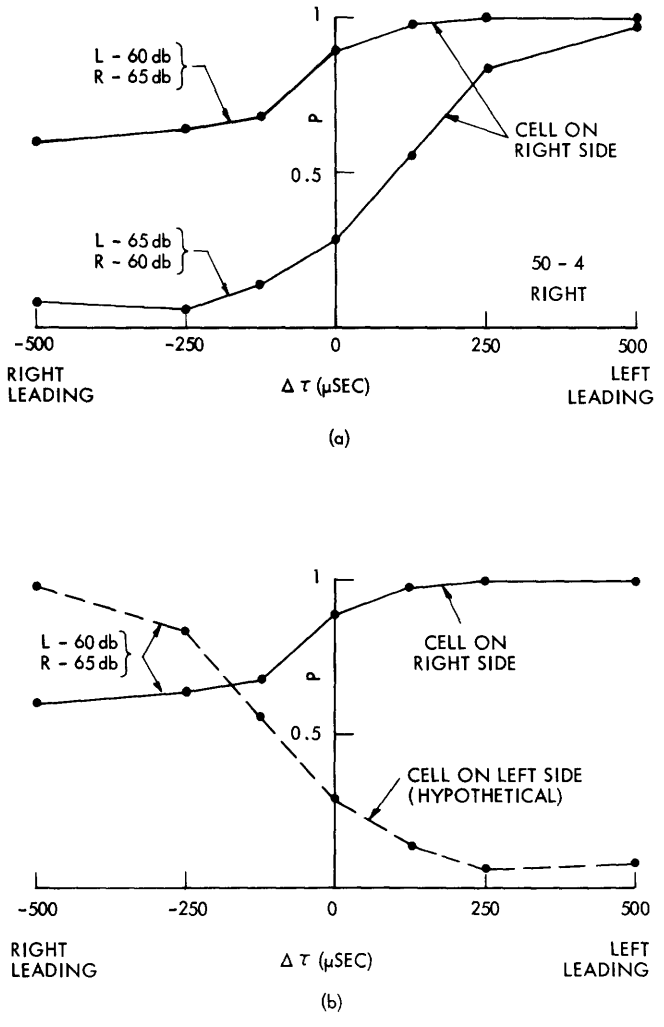


Fig. 19. Utilization of assumption of symmetry. Stimulus parameters for a cell on one side (a) are reversed, left and right, to obtain the activity of the hypothetical symmetrical cell on the opposite side (b).

and are estimated from the relative frequencies measured experimentally (see Appendix A). (Both P_I and P_C are obtained from data on one cell. We use the assumed property of symmetry to estimate the parameter for the contralateral population.)

If we assume that there are N cells in each accessory nucleus, then, for the stimulus configuration under consideration, the average numbers of cells responding in the ipsilateral and contralateral populations are NP_I and NP_C, respectively. We take as a measure of relative activity at the two sides the quantity R_I, defined as the average number of cells responding in the ipsilateral accessory nucleus population divided by the total number of cells responding in the ipsilateral and contralateral populations. (This is not the only possible measure of response activity at the two sides. For a discussion of another measure, see Scetion X and Appendix B.) Thus

$$R_I = \frac{NP_I}{NP_I + NP_C} = \frac{P_I}{P_I + P_C}.$$

R_C is similarly defined, and by the same reasoning

$$R_C = \frac{P_C}{P_I + P_C} = 1 - R_I.$$

In terms of the model, R_I (or R_C) is monotonically related to the degree of lateralization of the virtual image. Thus $0 \leq R_I < 0.5$ would result from greater response activity at the contralateral accessory nucleus than at the ipsilateral accessory nucleus; that is, the virtual image would be positioned to the ipsilateral side. The value $R_I = 0.5$ would result from identical activity at the ipsilateral and contralateral nuclei; that is, the virtual image would be at the midline. The value $0.5 < R_I \leq 1.0$ would result from greater activity at the ipsilateral accessory nucleus than at the contralateral accessory nucleus; that is, the virtual image would be to the contralateral side.

A specific example is given in Fig. 20. The two solid curves give values for P_I and P_C. (The cell actually observed was located on the ipsilateral side. P_C was obtained by using the assumption of symmetry.) The dashed line gives values for R_I determined from P_I and P_C. Note that the distance from the line $R_I = 0$ to the dashed line corresponds to R_I, and the distance from $R_I = 1$ to the dashed line corresponds to R_C.

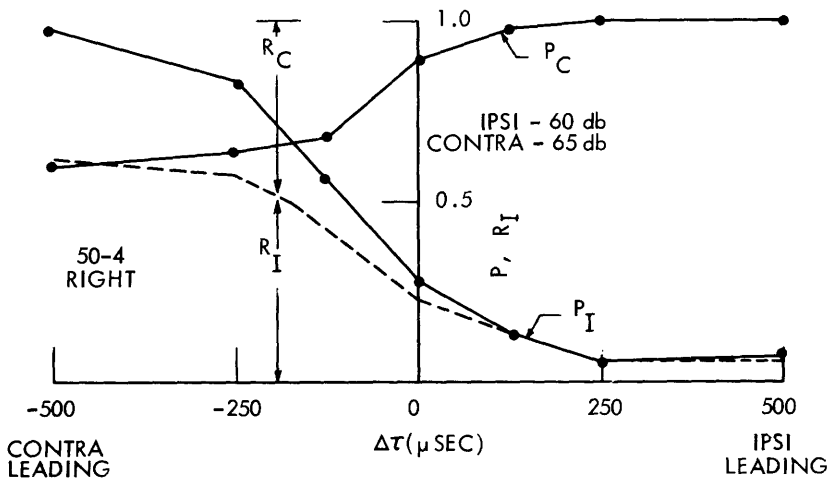


Fig. 20. Measure of relative amounts of activity in the ipsilateral and contralateral accessory nuclei, under the assumption that one cell is representative of both populations. $R_I = P_I/(P_I+P_C)$, where P_I is the relative frequency of firing of a cell in the ipsilateral accessory nucleus and P_C is the relative frequency of firing of a hypothetical symmetrical cell in the contralateral accessory nucleus. See Fig. 19 for explanation of how P_C is obtained from data on a cell actually in the ipsilateral accessory nucleus.

In subsequent sections we shall utilize the assumptions stated here to investigate the operation of the model with various combinations of intensity, interaural intensity difference, and interaural time difference, and to compare these results with results of psychophysical experiments on humans. Again a specific example: For the cell illustrated in Fig. 20, the stimulus to the ipsilateral ear is 5 db more intense than the stimulus to the contralateral ear. With zero interaural time difference, $R_I = 0.2$ – the virtual image is to the ipsilateral side. As the stimulus to the contralateral ear precedes the stimulus to the ipsilateral ear, R_I approaches 0.5 – the virtual image moves toward the midline. These results are in agreement with psychophysical experiments on humans.

The discussion above is based on the assumption that one cell is representative of all cells in the accessory olivary nuclei. This is an oversimplification. Even if we consider only the class of cells that we call "time-intensity trading" cells, all of the cells in the accessory nucleus do not belong to the same population. Such measures as threshold, and relative frequency of firing for a given stimulus situation, vary widely from one cell to another. This leads us to a different assumption, that the particular cells that we observed comprise a representative sample of the cells in the accessory nucleus. This assumption enables us to arrive at a measure of the total number of cells firing in the accessory nucleus by simply pooling the data from cells that we observed. This is the simplest possible assumption; we have no rationale for making any other. It is in error to the extent that we biased our sample by such factors as search stimulus, type of electrode, and location of recording sites. This we certainly have done, but, since we have no independent check on the distribution of populations, any other assumption could result only in loss of information.

If we assume that there are N cells in each accessory nucleus, and we have data on k cells, then the number of cells in each subpopulation would be $n = N/k$. If the probability of response of the cells in the i^{th} subpopulation in the ipsilateral accessory nucleus is P_{Ii} and the probability of response of the cells in the i^{th} subpopulation in the contralateral accessory nucleus is P_{Ci}, then the average number of cells in the i^{th} subpopulations in the ipsilateral and contralateral accessory nuclei responding to a given stimulus presentation are nP_{Ii} and nP_{Ci}, respectively. The total number of cells responding in the accessory nuclei on the two sides will be the sum of the numbers of cells responding in each of the subpopulations, or $\sum_{i=1}^{k} nP_{Ii}$ and $\sum_{i=1}^{k} nP_{Ci}$, respectively.

It is convenient in the following sections to use the symbols P_I and P_C to denote the averages of the P's of the subpopulations, as well as the P's of the subpopulations themselves. If we do so, it follows that $P_I = \frac{1}{k} \sum_{i=1}^{k} P_{Ii}$ and $P_C = \frac{1}{k} \sum_{i=1}^{k} P_{Ci}$. It is always clear from the context whether the P's are being used to refer to the probability of firing of a subpopulation or the average probability of firing of the subpopulations.

The measure of relative response activity in the ipsilateral and contralateral accessory nuclei will still be the average number of cells responding in the ipsilateral accessory nucleus divided by the total number of cells responding in the ipsilateral and

contralateral accessory nuclei. Thus

$$R_I = \frac{\sum_{i=1}^{k} nP_{Ii}}{\sum_{i=1}^{k} nP_{Ii} + \sum_{i=1}^{k} nP_{Ci}} = \frac{\frac{N}{k}\sum_{i=1}^{k} P_{Ii}}{\frac{N}{k}\sum_{i=1}^{k} P_{Ii} + \frac{N}{k}\sum_{i=1}^{k} P_{Ci}} = \frac{P_I}{P_I + P_C}.$$

Implicit in this equation is the additional assumption that we can pool data from a number of different cats. Only in very rare cases were we able to obtain data on more than five or six cells from a single preparation, so that it is impossible to demonstrate conclusively from our results that this pooling of data is legitimate. From what we have seen, it appears unlikely that response characteristics would be drastically different for different cats.

IX. EXPERIMENTAL RESULTS IN RELATION TO THE MODEL

In preceding sections we described a model for the process of binaural localization, based on the electrical activity of some cells in the accessory nucleus in response to click stimuli. In the following sections we present our experimental results and make comparisons between predictions of the model and results from human psychophysics. Implicit in this presentation are the assumptions that we made to relate the experimental data to the operation of the model.

We observed cell activity in response to three basic stimulus configurations: (1) as a function of average intensity and interaural time difference, with interaural intensity difference equal to 0 db (average intensity is average of the intensity of the stimuli at the ipsilateral and contralateral ears, expressed in decibels); (2) as a function of average intensity and interaural intensity difference, with interaural time difference equal to 0 μsec; (3) as a function of average intensity and interaural time difference, with interaural intensity difference equal to 5 db.

The only cells considered are the "time-intensity trading" cells of section 7.3. They represent a majority, but by no means all, of the cells showing binaural interaction.

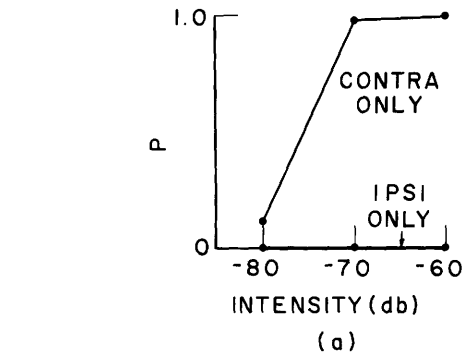
9.1 EFFECT OF AVERAGE INTENSITY AND INTERAURAL TIME DIFFERENCE (INTERAURAL INTENSITY DIFFERENCE EQUAL TO 0 db)

The distance between the two ears of a cat is approximately 7.5 cm. This corresponds to a maximum interaural time difference in free-field stimulation of approximately 250 μsec. Accordingly, we observed relative frequency of firing of cells with interaural time differences up to 250 μsec or 500 μsec. Preliminary experiments indicated that there was little "fine structure" in curves of relative frequency of firing versus interaural time difference; thus we usually did not make measurements at differences in interaural time difference of less than 125 μsec.

We attempted to obtain measurements over as wide a range of intensity as possible. Occasionally at high intensity the spike potential would be lost in the slow-wave potential, thereby making acquisition of data impossible. Often the cell would be lost through movement of the electrode relative to the brain. Only cells that exhibited stable responses, as described in section 7.3, are reported on here.

Graphs showing the relative frequency of firing P as a function of interaural time difference $\Delta\tau$ for three individual cells are shown in Figs. 21-23. Average intensity appears as a parameter. In each case the monaural intensity function is included for comparison. We observe the convention of calling $\Delta\tau$ positive when the stimulus to the ipsilateral ear leads and negative when the stimulus to the contralateral ear leads.

We have chosen these three cells as examples because they typify the range of properties that we observed in time-intensity trading cells. The cell of Fig. 21 fired 6 times out of 50 in response to clicks presented to the contralateral ear at -80 db and 49 times out of 50 in response to clicks presented to the contralateral ear at -70 db. At higher



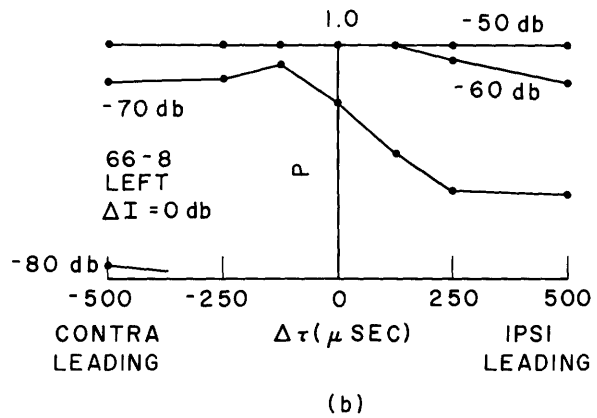
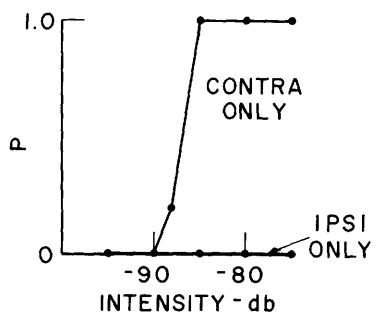


Fig. 21.

Cell 66-8: Effect of average intensity and interaural time difference on relative frequency of firing P. (a) Monaural. (b) Binaural. Cell on left side. Interaural intensity difference, 0 db.



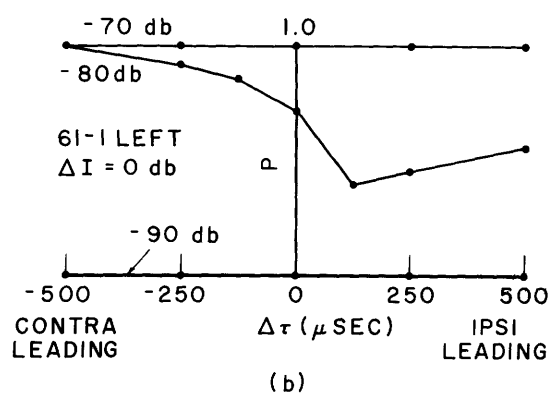


Fig. 22.

Cell 61-1: Effect of average intensity and interaural time difference on relative frequency of firing P. (a) Monaural. (b) Binaural.

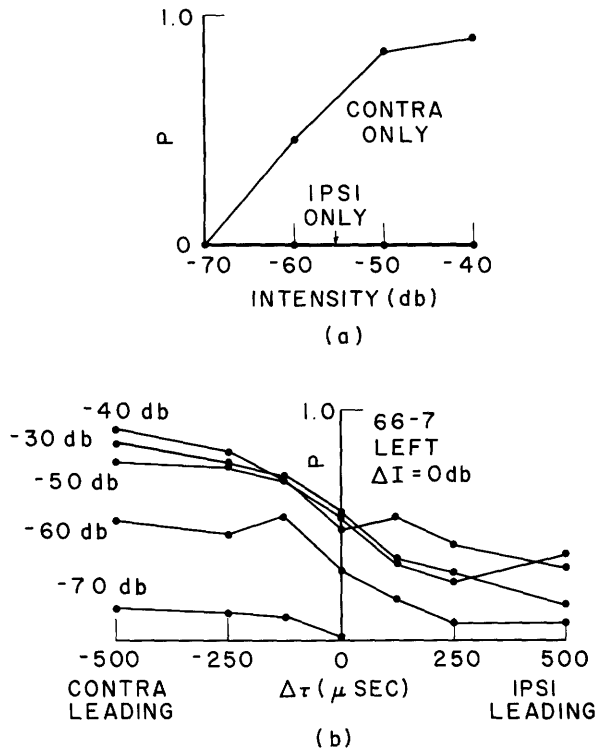


Fig. 23. Cell 66-7: Effect of average intensity and interaural time difference on relative frequency of firing P. (a) Monaural. (b) Binaural.

intensities it fired in response to every stimulus presentation. It did not fire in response to clicks presented to the ipsilateral ear. When clicks were presented to both ears, the cell responded to essentially every stimulus presentation at intensities of -50 db and above, no matter what the interaural time difference. At intensities of -80 db and below, the cell did not respond. At intermediate intensities, the activity of the cell was a function of the interaural time difference. The relative frequency of firing decreased when the stimulus to the ipsilateral ear led.

The cell of Fig. 22 was somewhat more sensitive than the cell just described and showed a more abrupt increase in firing with increase in intensity of the stimulus. This is reflected in the activity under binaural stimulation. The cell did not respond at all at intensities of -90 db and below and responded to every stimulus presentation at intensities of -70 db and above, a change of only 20 db. Again, the relative frequency of firing decreased when the stimulus to the contralateral ear led. The increase in relative frequency of firing between $\Delta\tau = +125$ μsec and $\Delta\tau = +500$ μsec is atypical and can possibly be ascribed to sampling error (see Appendix A).

The cell of Fig. 23 showed a number of differences from the cells already described. The monaural intensity function was quite gradual, and even at high intensities the cell did not respond to every stimulus presentation. With binaural stimuli, the cell showed the same change in relative frequency of firing with changes of interaural time difference which we have already described. The difference is that at intensities above -50 db the relative frequency of firing did not change with changes of intensity, but appeared to reach an asymptote.

In order to obtain a measure of the average probability of firing in the ipsilateral and contralateral accessory nuclei, we pooled data from a number of individual cells. The significance of P and R_I as applied to the pooled data is explained in section 8.2. Three groups of cells are considered, each group covering a different range of average intensities. We shall refer to these three groups as groups A, B, and C. The composition of the three groups of cells is as

follows: Group A: -50 db, -60 db, -70 db, -80 db, 14 cells. Group B: -40 db, -50 db, -60 db, 12 cells, eleven of which are also in group A. Group C: -30 db, -40 db, -50 db, 9 cells, seven of which are also in both groups A and B. In essence, we are

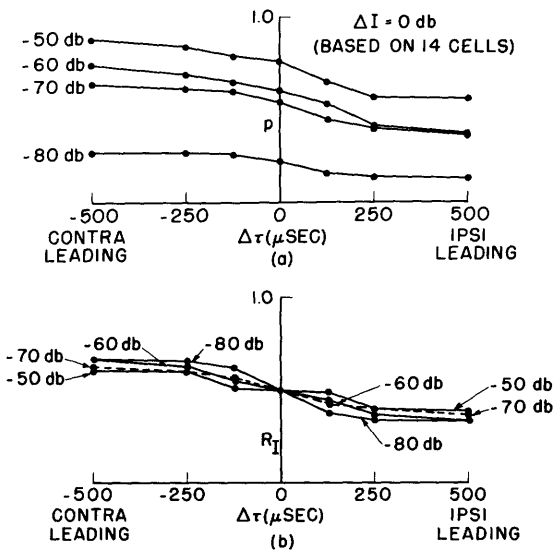


Fig. 24.

Group A: Combined activity of 14 cells. Effect of average intensity and interaural time difference. (a) Average probability of firing P. (b) Relative amount of activity R_I.

compromising between including all cells for which we have data at a given intensity, thereby including the maximum number of cells but being unable to make comparisons across intensities, and including only cells from which we have data over the entire

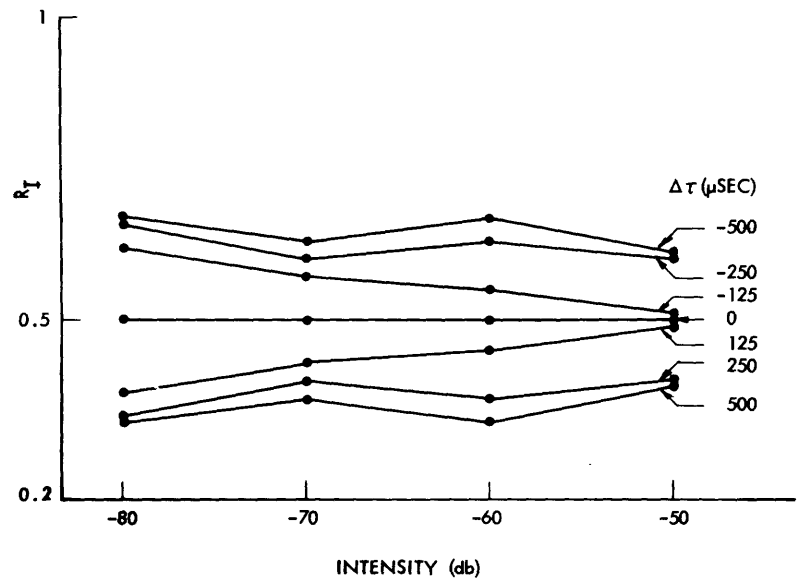


Fig. 25. Group A: Combined activity of 14 cells. Effect of average intensity and interaural time difference on R_I. Same data as Fig. 24 plotted against average intensity.

range of intensities, thereby being able to make comparisons across the entire range of intensities but restricting ourselves to very few cells.

The average probability of firing computed from the cells of group A is shown in Fig. 24a. As explained in Section VIII, P in this figure is the average probability of firing of the cells in this group and is equal to $\frac{1}{14}\sum_{i=1}^{14} P_i$, where the P_i's are the relative frequencies of firing of the 14 cells in the group. The average probability of firing is a function of both interaural time difference and average intensity. The average probability of firing increases as the stimulus to the contralateral ear precedes the stimulus to the ipsilateral ear, and it increases as average intensity increases.

Our measure of the relative amounts of response activity in the ipsilateral and contralateral accessory nuclei, R_I, is plotted in Fig. 24b. These curves are computed directly from Fig. 24a, as explained in Section VIII. Figure 24b as we have drawn it is redundant because of the assumed property of symmetry. Since there is no interaural intensity difference, P_I for a given $\Delta\tau$ is identical to P_C for $-\Delta\tau$ (same interaural time difference, relative position of the stimuli to ipsilateral and contralateral ears interchanged). It follows that R_I for a given $\Delta\tau$ is identical to $1 - R_I$ for $-\Delta\tau$.

With zero interaural time difference ($\Delta\tau=0$), R_I is 0.5. As the stimulus to the ipsilateral ear precedes the stimulus to the contralateral ear ($\Delta\tau > 0$), R_I decreases. Although R_I is a function of interaural time difference, it is not to any great extent a function of average intensity. This is more apparent in Fig. 25, in which the data of Fig. 24b is replotted against intensity, with interaural time difference as a parameter. There may possibly be a consistent trend with $\Delta\tau$ = 125 μsec; there is no obvious relationship between R_I and intensity for other values of $\Delta\tau$.

Average probabilities of firing P from group B are shown in Fig. 26a. As with group A, P increases as the stimulus to the contralateral ear precedes the stimulus to the ipsilateral ear. P increases as the average intensity increases from -60 db to -50 db; it also increases as the average intensity increases from -50 db to -40 db, but by a smaller amount. This is to be expected, since our sample is composed of cells such as those shown in Figs. 21-23, and the relative frequency of firing of these cells remains constant with changes of intensity above a certain intensity.

R_I computed from the data of Fig. 26a is shown in Fig. 26b. Again, many of the same features appear here as appeared in Fig. 24b. R_I is equal to 0.5 for $\Delta\tau$ = 0, is less than 0.5 for $\Delta\tau$ greater than zero, and is greater than 0.5 for $\Delta\tau$ less than zero. As in Fig. 24b, R_I appears to be a function of interaural time difference and not a function of average intensity.

Average probabilities of firing from group C are shown in Fig. 27a. Over this range of intensities almost all of the cells in the sample have reached their maximum relative frequencies of firing, and P does not change with increasing intensity. R_I, shown in Fig. 27b, is essentially identical for the three intensities considered.

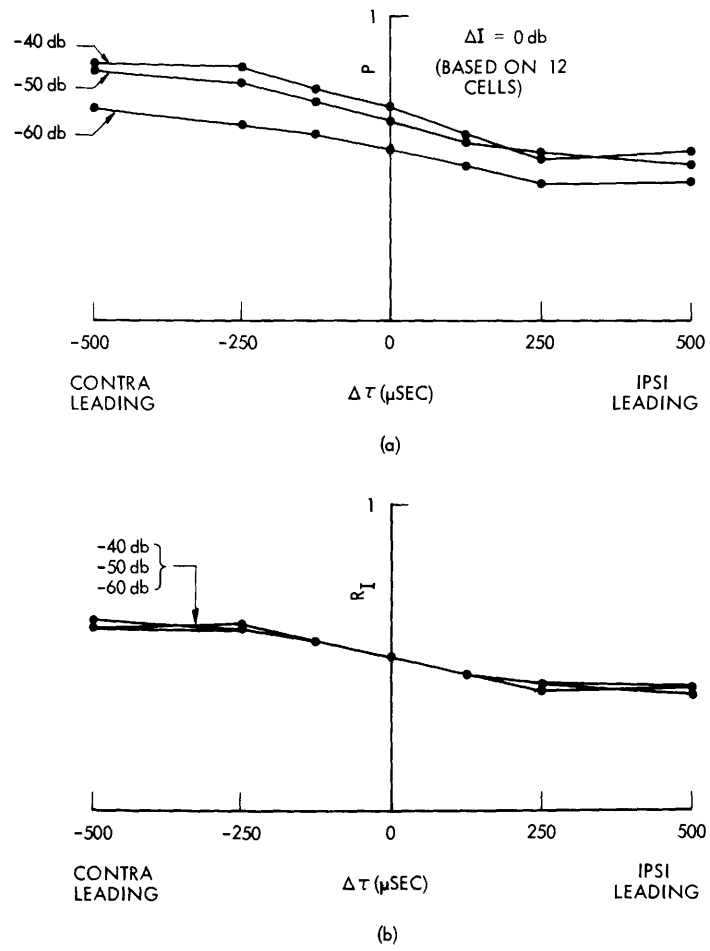


Fig. 26. Group B: Combined activity of 12 cells. Effect of average intensity and interaural time difference. (a) Average probability of firing P. (b) Relative amount of activity R_I.

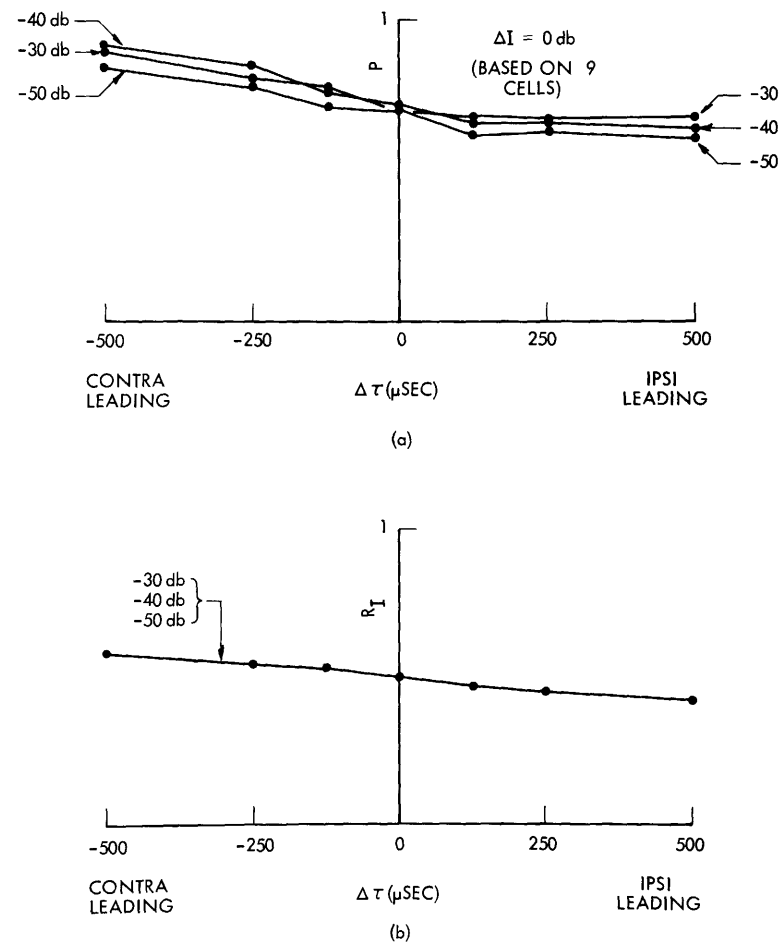


Fig. 27. Group C: Combined activity of 9 cells. Effect of average intensity and interaural time difference. (a) Average probability of firing P. (b) Relative amount of activity R_I.

9.2 EFFECT OF AVERAGE INTENSITY AND INTERAURAL INTENSITY DIFFERENCE (INTERAURAL TIME DIFFERENCE EQUAL TO 0 μsec)

The maximum interaural intensity difference obtained in free-field stimulation in humans is of the order of 10 db, the value depending on the frequency of the stimulus.[78] Accordingly, we used stimuli with interaural intensity differences of 0 db, ±4 db, and ±8 db. In every case we varied the intensities of the stimuli at the two ears symmetrically about the average intensity, in order to keep the average intensity constant. The sign convention is ΔI positive for stimulus to the ipsilateral ear more intense, ΔI negative for stimulus to the contralateral ear more intense.

Graphs showing relative frequency of firing P as a function of interaural intensity difference ΔI for three individual cells are shown in Figs. 28-30. These are the same cells shown in Figs. 21-23, and many of the same comments apply.

The cell of Fig. 28 responded to essentially every stimulus presentation when the average intensity was equal to or greater than −50 db, no matter what the interaural

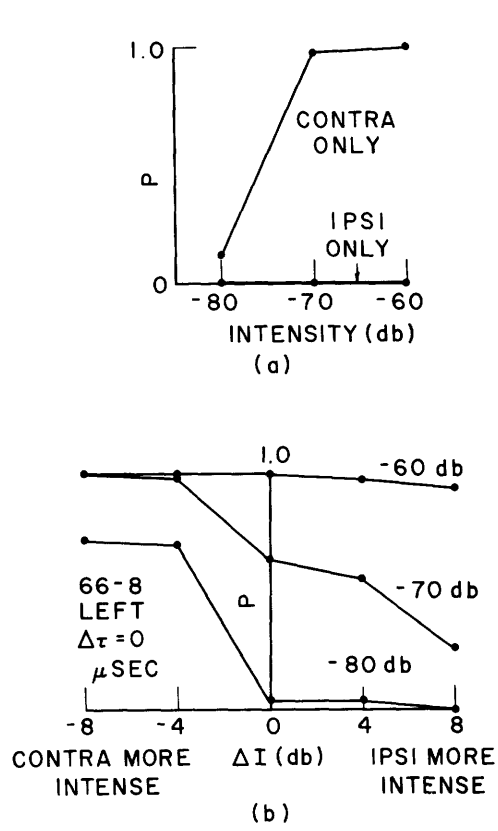


Fig. 28. Cell 66-8: Effect of average intensity and interaural intensity difference on relative frequency of firing P. (a) Monaural. (b) Binaural.

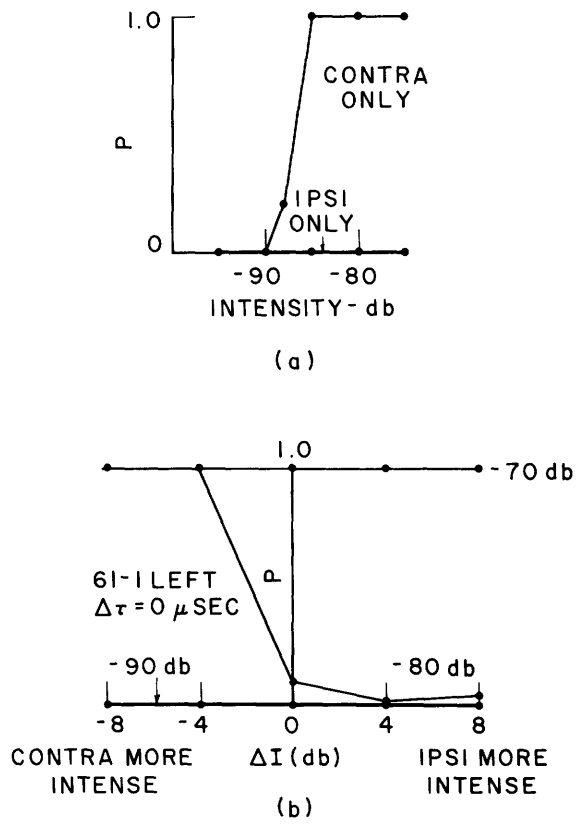


Fig. 29. Cell 61-1: Effect of average intensity and interaural intensity difference on relative frequency of firing P. (a) Monaural. (b) Binaural.

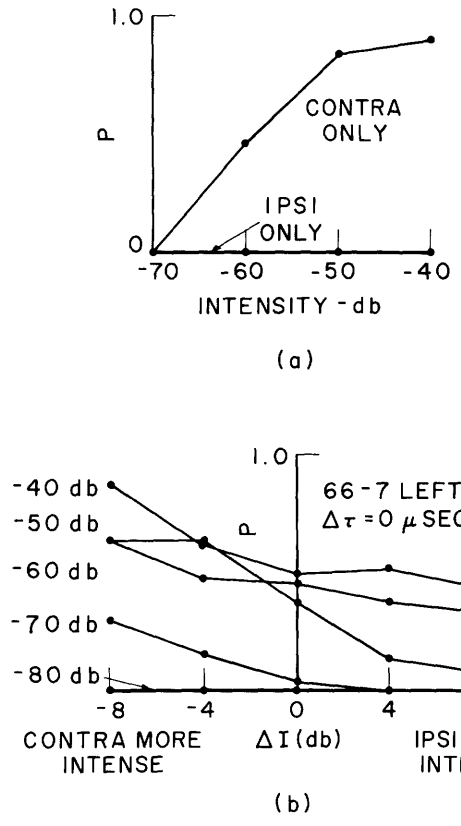


Fig. 30. Cell 66-7: Effect of average intensity and interaural intensity difference on relative frequency of firing P. (a) Monaural. (b) Binaural.

intensity difference. When the average intensity was equal to or less than -80 db, the cell did not respond. At intermediate average intensities, the relative frequency of firing was a function of the interaural intensity difference. The relative frequency of firing decreased when the stimulus to the ipsilateral ear was more intense.

This change of relative frequency of firing with interaural intensity difference can be ascribed in part to monaural effects. The interaural intensity difference was produced by changing the intensity of the stimuli to both ears in order to keep average intensity constant. As the intensity of the stimulus to the ipsilateral ear became greater than the intensity of the stimulus to the contralateral ear, the absolute intensity of the stimulus to the contralateral ear decreased. Even in the absence of binaural interaction, this would result in a decrease of relative frequency of firing, as shown in the monaural intensity functions of Fig. 28a. We can ascertain that there was binaural interaction present by making two comparisons: First, the relative frequency of firing at the point I = -70 db, ΔI = 0 db (that is, ipsilateral intensity -70 db, contralateral intensity -70 db) was less than the relative frequency of firing with a -70-db click presented only to the contralateral ear. Second, the relative frequency of firing at the point I = -70 db, ΔI = +8 db (that is, ipsilateral intensity -66 db, contralateral intensity -74 db) was less than the relative frequency of firing at the point I = -80 db, ΔI = -8 db (that is, ipsilateral intensity -84 db, contralateral intensity -76 db), even though the absolute intensity of the stimulus to the contralateral ear was greater. The stimulus to the ipsilateral ear was indeed exerting an inhibitory influence, and the amount of inhibition depended on the intensity.

The cell of Fig. 29 was somewhat more sensitive than the cell just described and went from a relative frequency of firing of zero to a relative frequency of firing of one over a smaller range of average intensity, both monaurally and binaurally. This parallels the activity of the same cell with interaural time difference, shown in Fig. 22.

The cell of Fig. 30 differed from the preceding two cells with interaural intensity difference in exactly the same way as it did with interaural time difference (Fig. 23).

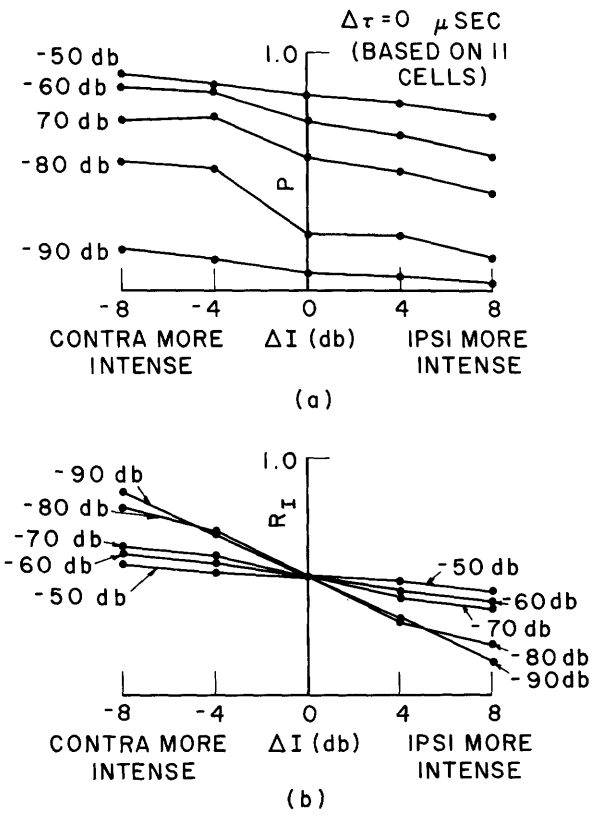


Fig. 31. Group D: Combined activity of 11 cells. Effect of average intensity and interaural intensity difference. (a) Average probability of firing P. (b) Relative amount of activity R_I.

It showed change in activity over a wider range of average intensity, and above approximately -50 db its relative frequency of firing was little affected by changes in intensity.

We again pooled data from a number of different cats in order to obtain a measure of the average probability of firing. Two groups of cells are considered, each group covering a different range of average intensities. We shall refer to these two groups as groups D and E. The composition of the two groups of cells is as follows: Group D: average intensities -50 db, -60 db, -70 db, -80 db, and -90 db, 11 cells. Group E: average intensities -40 db and -50 db, 13 cells, nine of which are also in group D. There is partial, but not complete, overlap between cells used in interaural time difference measurements (groups A, B, and C) and cells used in interaural intensity difference measurements (groups D and E).

The average probabilities of firing computed from the cells of group D are shown in Fig. 31a. The average probability of firing is a function of both average intensity and interaural intensity difference. Relative frequency of firing increases as average intensity increases, and increases as the stimulus to the contralateral ear is made more intense than the stimulus to the ipsilateral ear.

R_I computed from the data of Fig. 31a is shown in Fig. 31b. As was the case with interaural time difference, Fig. 31b is redundant because of the assumed property of symmetry. R_I for a given ΔI is identical to $1 - R_I$ for $-\Delta I$ (same interaural intensity difference, intensities at the ipsilateral and contralateral ears reversed).

With zero interaural intensity difference ($\Delta I=0$), R_I is 0.5. When the stimulus to the ipsilateral ear is more intense than the stimulus to the contralateral ear ($\Delta I>0$), R_I is less than 0.5. As the interaural time difference becomes more positive, R_I becomes smaller. These results parallel the findings with interaural time difference and no interaural intensity difference.

There is a striking difference between the two sets of results in the effect of average

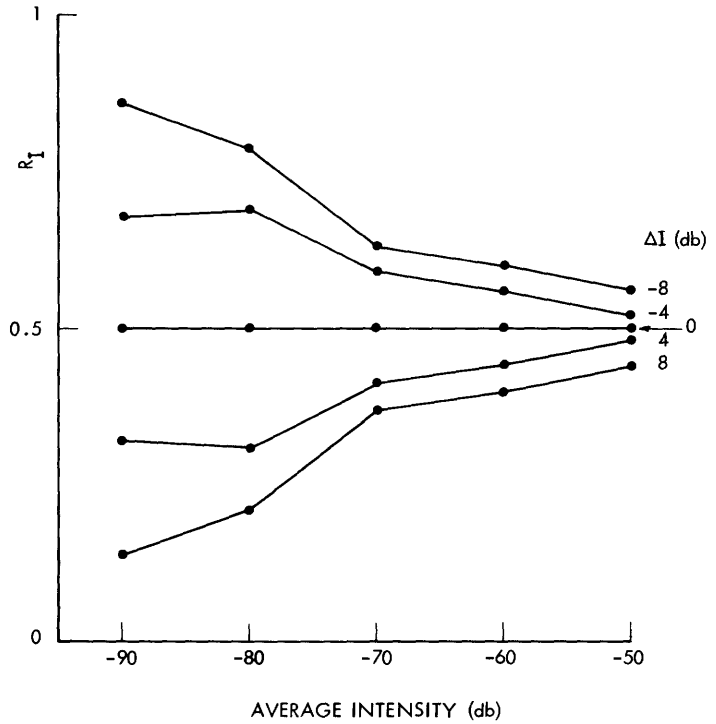


Fig. 32. Group D: Combined activity of 11 cells. Effect of average intensity and interaural intensity difference on R_I. Same data as Fig. 31 plotted against average intensity.

intensity on R_I, with the interaural intensity difference held constant. As the average intensity increases, R_I draws closer to the value 0.5. The results of Fig. 31b are plotted against average intensity in Fig. 32 to show this effect more clearly.

The average probabilities of firing from group E are shown in Fig. 33a. As with group D, P is a function of interaural intensity difference. As the stimulus to the contralateral ear is made more intense, P increases. Increase of average intensity has little effect on P. For some values of interaural intensity difference, P is actually smaller at −40 db than it is at −50 db. We observed a similar effect in Fig. 27a, and for just the same reason. Almost all of the cells in the sample have reached their maximum relative frequency of firing, and P does not change with increasing intensity.

R_I computed from the data of Fig. 33a is shown in Fig. 33b. As in Fig. 31b, R_I is less than 0.5 for stimulus to the ipsilateral ear more intense, and the effect on R_I of a given interaural intensity difference decreases with an increase of average intensity.

9.3 EFFECT OF AVERAGE INTENSITY AND INTERAURAL TIME DIFFERENCE (INTERAURAL INTENSITY DIFFERENCE EQUAL TO 5 db)

A well-studied phenomenon in psychophysics is the time-intensity trading effect. If impulsive stimuli are presented binaurally to a human observer with both an interaural

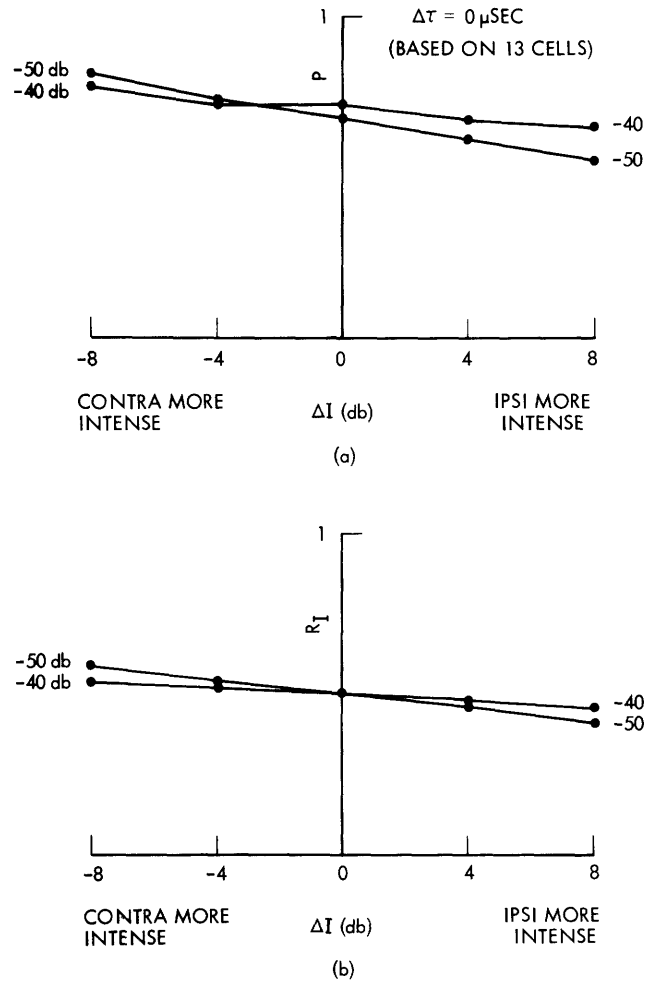


Fig. 33. Group E: Combined activity of 13 cells. Effect of average intensity and interaural intensity difference. (a) Average probability of firing P. (b) Relative amount of activity R_I.

time difference and an interaural intensity difference, under certain conditions the time and intensity differences can be made to offset each other, and the virtual image appears at the midline.

In terms of the model, a centered virtual image results when there is equal response activity in the ipsilateral and contralateral accessory nuclei. In sections 9.1 and 9.2 there is, by definition, equal response activity in the ipsilateral and contralateral accessory nuclei when both ΔI and $\Delta\tau$ are equal to zero, because of the assumed property of symmetry. In order to obtain electrophysiological data comparable to the time-intensity trading effect in psychophysics, we kept the interaural intensity difference constant at 5 db and varied the interaural time difference over the range from +500 μsec to -500 μsec.

Results from a typical cell for monaural stimulation are shown in Fig. 34a. The cell

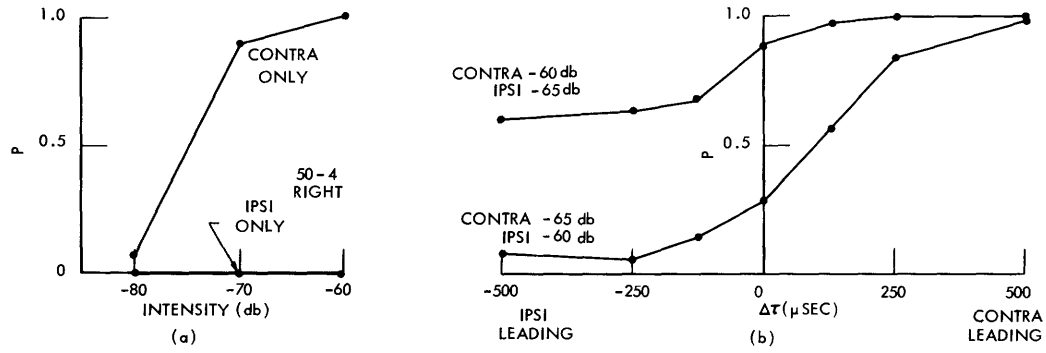


Fig. 34. Cell 50-4: Effect of interaural time difference with 5-db interaural intensity difference. (a) Monaural. (b) Binaural.

did not respond to monaural stimulation of the ipsilateral ear but did respond to monaural stimulation of the contralateral ear. The relative frequency of firing increased as the intensity of the stimulus to the contralateral ear increased.

The relative frequency of firing of this cell as a function of interaural time difference and interaural intensity difference is shown in Fig. 34b for an average intensity of -62.5 db. Interaural time difference, from contralateral leading by 500 μsec to ipsilateral leading by 500 μsec, is plotted on the abscissa. Two interaural intensity difference conditions are shown: contralateral -65 db, ipsilateral -60 db, and the symmetrical condition contralateral -60 db, ipsilateral -65 db. The effects of interaural time difference and of interaural intensity difference taken separately were just the same for this cell as they were for the cells discussed in the preceding two sections. The relative frequency of firing was greater when the stimulus to the contralateral ear led than when the stimulus to the ipsilateral ear led, with the intensity relationships held constant; and the relative frequency of firing was greater when the stimulus to the contralateral ear was more intense than when the stimulus to the ipsilateral ear was more intense, with the timing relationships held constant.

We have described only one cell at one average intensity. This cell is typical of the cells that we observed. As did the three cells described in sections 9.1 and 9.2, the cells that we observed showed some variation in sensitivity to parameter changes.

Once again we partition the cells into groups. The composition of the groups is as follows: Group F: average intensities -52.5 db, -62.5 db, -72.5 db, -82.5 db, 13 cells. Group G: average intensities -32.5 db, -42.5 db, -52.5 db, -62.5 db, 7 cells, six of which are also in group F.

The average probabilities of firing computed on the basis of the cells of group F are shown in Fig. 35. The results are similar for each intensity shown. The average probability of firing is larger when the stimulus to the contralateral ear is more intense or arrives earlier.

R_I is computed from these results in the same manner as before. Now "ipsilateral" and "contralateral" are reversed for both intensity and time, as shown in Fig. 36 for the

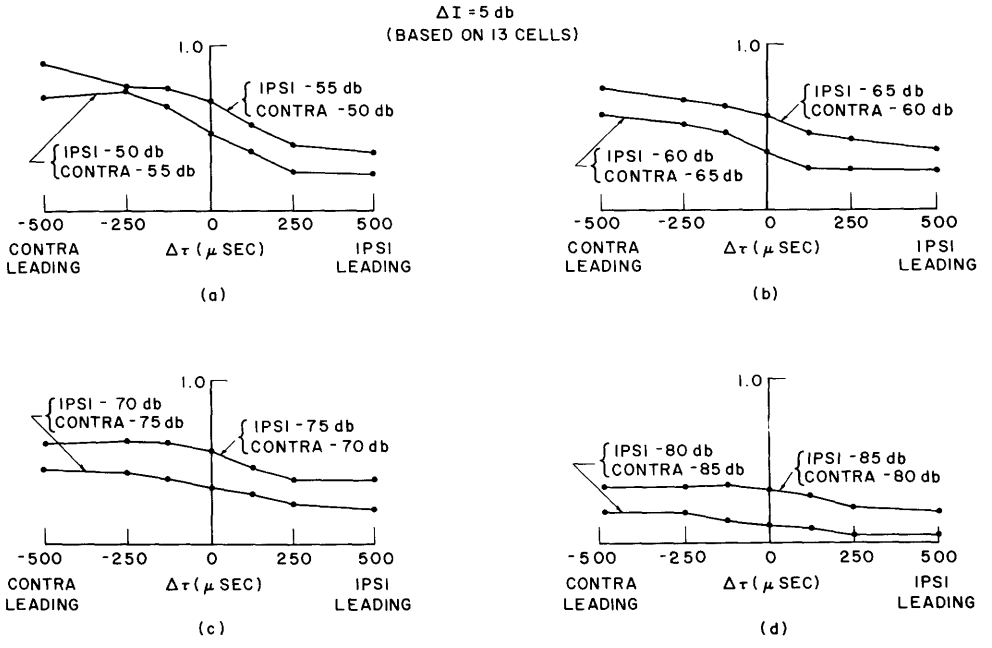


Fig. 35. Group F: Combined activity of 13 cells. Effect of average intensity and interaural time difference on average probability of firing P. Interaural intensity difference, 5 db.

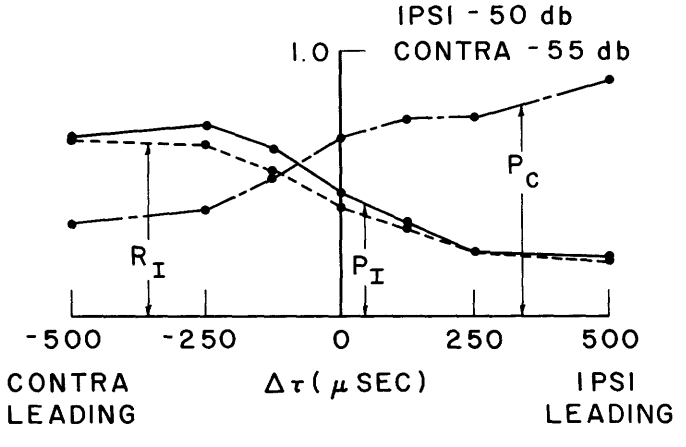


Fig. 36. Group F: Combined activity of 13 cells. Example of determination of R_I from data of Fig. 35.

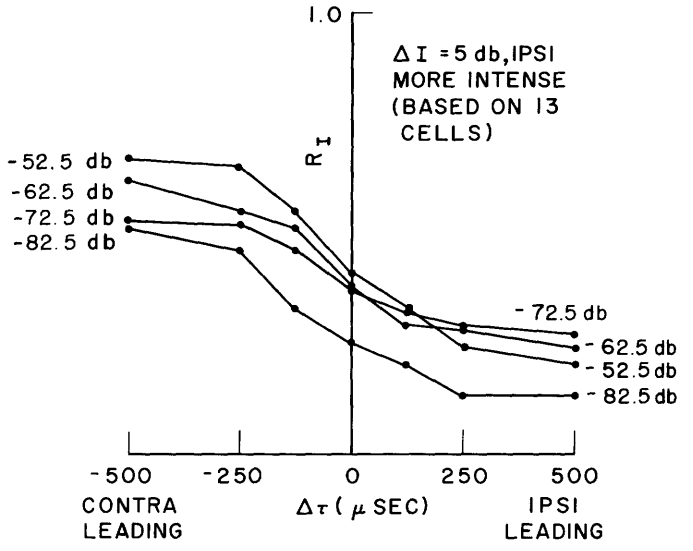


Fig. 37. Group F: Combined activity of 13 cells. Effect of average intensity and interaural time difference on relative amount of activity R_I. Interaural intensity difference, 5 db; ipsilateral stimulation more intense than contralateral.

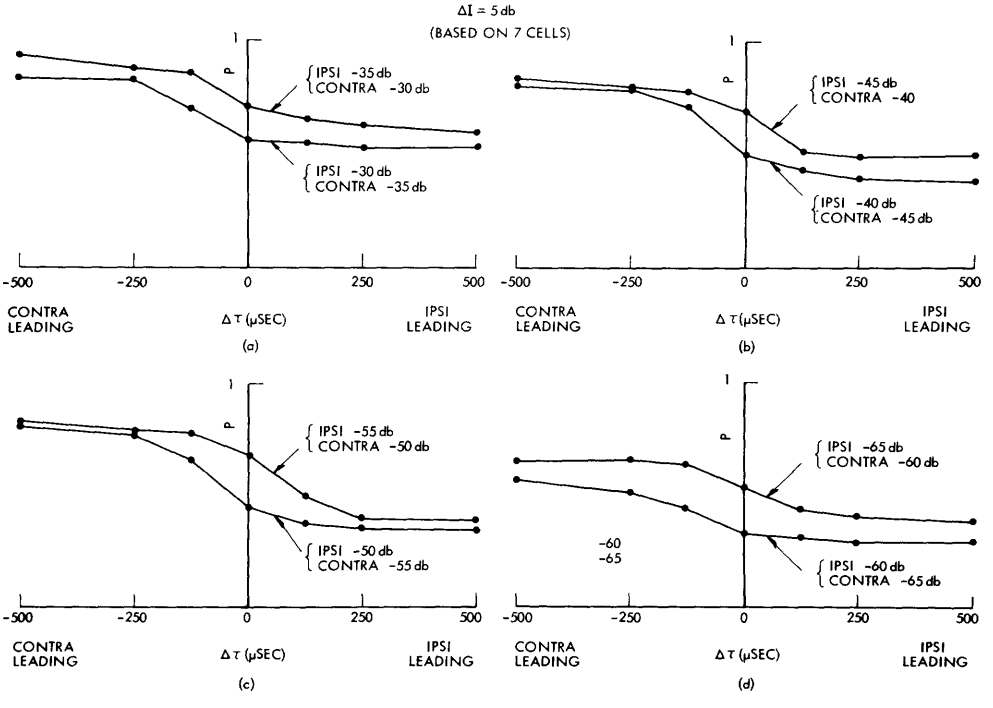


Fig. 38. Group G: Combined activity of 7 cells. Effect of average intensity and interaural time difference on average probability of firing P. Interaural intensity difference, 5 db.

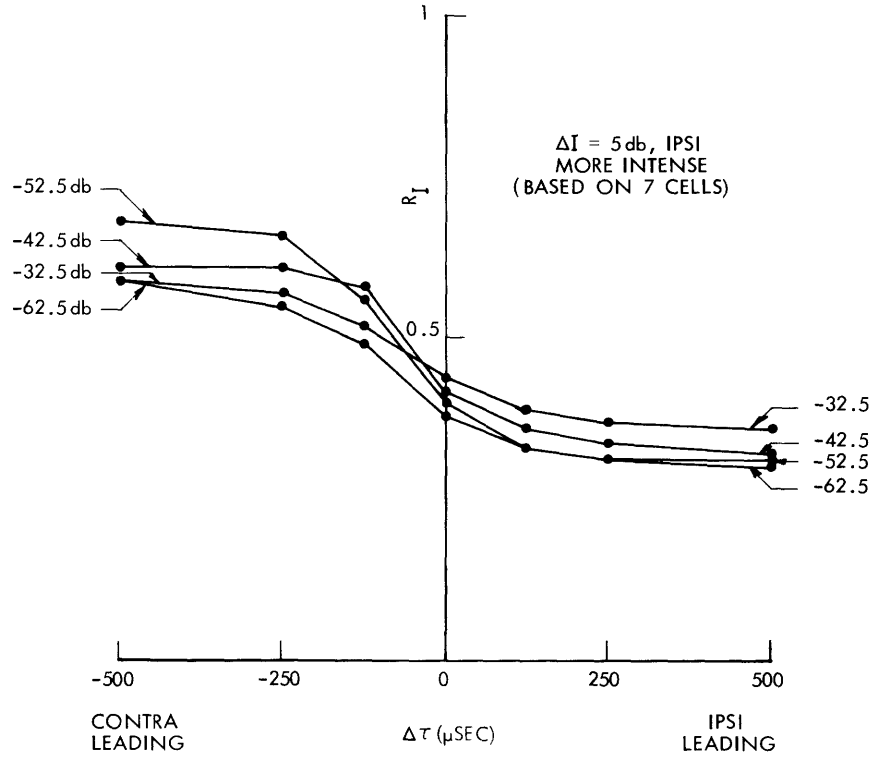


Fig. 39. Group G: Combined activity of 7 cells. Effect of average intensity and interaural time difference on relative amount of activity R_I. Interaural intensity difference, 5 db.

single average intensity -52.5 db.

R_I computed from the data of Fig. 35 is shown in Fig. 37 as a function of interaural time difference, with average intensity as a parameter. Since the stimulus to the ipsilateral ear is 5 db more intense than the stimulus to the contralateral ear, R_I is less than 0.5 when the interaural time difference is zero. Furthermore, this constant interaural intensity difference produces a larger deviation of R_I from the value 0.5 at low intensities than it does at high intensities, in qualitative agreement with the results of section 9.2.

The average probabilities of firing computed on the basis of the cells of group G are shown in Fig. 38. Once again, P is larger when the stimulus to the contralateral ear is more intense or arrives earlier than the stimulus to the ipsilateral ear.

R_I computed from the data of Fig. 38 is shown in Fig. 39. With zero interaural time difference, the constant interaural intensity difference has a greater effect at low average intensities than it does at high.

9.4 DISCUSSION OF EXPERIMENTAL RESULTS

In sections 9.1-9.3 we presented the results of observations of activity of nerve cells in the accessory nucleus in response to binaurally presented clicks. In this section we

consider these empirical results in terms of the model in order to make comparisons between predictions of the model and results from human psychophysics.

Figures 24b and 31b present results not in conflict with our knowledge of the psychophysics of binaural localization. In both figures, R_I is equal to 0.5 when both the interaural time difference and the interaural intensity difference are equal to zero. (This occurs as a result of the way in which we formulated the model. Because of the assumed property of symmetry, there is, by definition, equal response activity in the ipsilateral and contralateral accessory nuclei when the stimuli at the two ears are identical.) In terms of the model, for R_I equal to 0.5 the virtual image is positioned at the midline, in agreement with results of psychophysical experiments. As the stimulus to the ipsilateral ear precedes the stimulus to the contralateral ear (Fig. 24b) or is more intense than the stimulus to the contralateral ear (Fig. 31b), R_I decreases, and in terms of the model the virtual image is positioned to the ipsilateral side of the midline. As $\Delta\tau$ or ΔI becomes still more positive, R_I decreases still further, and in terms of the model the virtual image is positioned further off center. These results parallel results from human psychophysics.

The change of R_I with change in $\Delta\tau$ is more rapid for values of $\Delta\tau$ less than 250 μsec than it is for values of $\Delta\tau$ greater than 250 μsec. It is tempting to draw the conclusion that the position of the virtual image changes more rapidly with changes in $\Delta\tau$ for small $\Delta\tau$ than for large. This could then be identified with the Hornbostel-Wertheimer constant[38] as observed in humans. This line of reasoning is unjustified. R_I is a measure of the relative amounts of activity in the ipsilateral and contralateral accessory nuclei, and nothing more. Although in terms of the model R_I tells us whether the virtual image is at the midline or off to one side or the other, it does <u>not</u> tell us how far the virtual image is from the midline. In particular, we have no reason to believe that R_I and the position of the virtual image are linearly related.

A somewhat weaker statement is that the position of the virtual image is uniquely related to R_I. That is, if two different stimulus configurations result in the same value of R_I, then these two stimulus configurations would also result in the same position of the virtual image. With the assumption that this is indeed the case, we are able to make comparisons across intensities.

As is shown in Figs. 25 and 32, R_I does not change when the average intensity changes if the interaural intensity difference is equal to zero and the interaural time difference is not equal to zero, while R_I does change when the average intensity changes if the interaural time difference is equal to zero and the interaural intensity difference is not equal to zero. If our assumption that R_I is uniquely related to the position of the virtual image is justified, this would indicate that with zero interaural intensity difference the position of the virtual image is a function only of interaural time difference and not of average intensity, although with zero interaural time difference and fixed interaural intensity difference the virtual image is closer to the midline at high average intensity than at low.

The analogous results from psychophysics are inconclusive. One author[50] states that the position of the virtual image with zero interaural intensity difference and a constant interaural time difference does depend on average intensity, and another author[49] states that it does not. In time-intensity trading experiments, a larger interaural intensity difference is required to offset a given interaural time difference at high average intensity than at low.[51] This is consistent with – but does not require – the prediction of the model that a given interaural intensity difference should have less effect on position of the virtual image at high average intensity than at low.

The time-intensity trading ratio in typical psychophysical experiments is obtained by presenting the subject with clicks that have a fixed nonzero interaural intensity difference and requiring the subject to adjust the interaural time difference until the virtual image is at the midline. The resulting time difference is then divided by the interaural intensity difference to obtain a number with the dimensions of microseconds per decibel, which is called the time-intensity trading ratio. Our procedure for obtaining a time-intensity trading ratio from the electrophysiological data is quite similar. We presented the cat with clicks that had a fixed nonzero (5 db) interaural intensity difference and determined the interaural time difference at which there is equal response activity in the ipsilateral and contralateral accessory nuclei ($R_I = 0.5$). This interaural time difference was then divided by 5 db to obtain the time-intensity trading ratio.

We can determine the interaural time difference required to offset an interaural intensity difference of 5 db by scanning along the line $R_I = 0.5$ in Figs. 37 and 39. In terms of the model, $R_I = 0.5$ results in a centered virtual image, no matter from what combination of interaural time and intensity differences it may result, because (on the average) when $R_I = 0.5$ there is equal response activity in the ipsilateral and

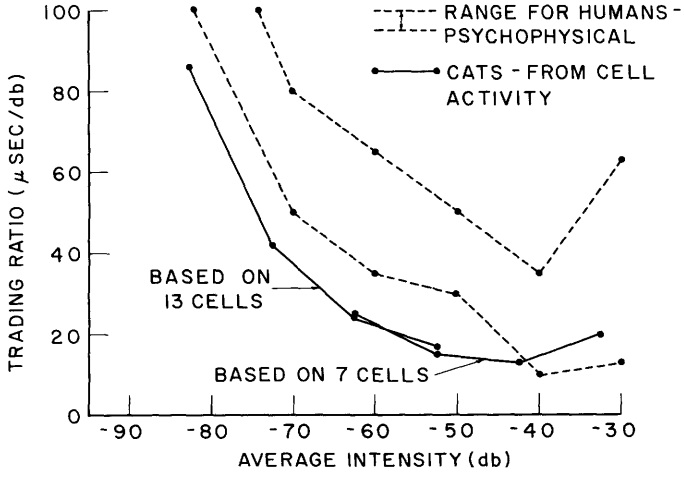


Fig. 40. Time-intensity trading ratio computed on basis of model. The dotted lines indicate the range of time-intensity trading ratios observed in centering experiments on humans.[51]

contralateral accessory nuclei. In this case, the stimulus to the ipsilateral ear is more intense, thereby making R_I less than 0.5, but this can be offset by making the stimulus to the contralateral ear arrive earlier.

The time-intensity trading ratio predicted by the model is plotted as a function of average intensity in Fig. 40. Two curves are shown, one based on group F (Fig. 37) and one based on group G (Fig. 38). The analogous results from centering experiments with humans are given for comparison. There is a remarkable degree of similarity between the two sets of results obtained from two different species by quite diverse methods. The time-intensity trading ratio determined from psychophysical experiments in the manner described above increases as average intensity decreases, and so does the time-intensity trading ratio determined on the basis of the electrophysiological results. The trading ratios predicted by the model are approximately as large as trading ratios obtained from human psychophysics.

X. MINIMUM DETECTABLE CHANGES PREDICTED BY THE MODEL

10.1 INTRODUCTION

A final topic that we wish to investigate is the precision that could be afforded by the model in detecting small changes of interaural time difference or interaural intensity difference. This will be treated in terms analogous to the following two-alternative forced-choice psychophysical experiment: A pair of clicks is presented to the two ears of a human observer with some interaural time difference or some interaural intensity difference. Subsequently, a second pair of clicks is presented with a slightly different time or intensity difference. The observer is required to report the apparent direction of the change in the position of the virtual image as being to the left or to the right. The precision of the observer in detecting changes in interaural time or intensity difference is then identified with the change in time or intensity difference at which he is "correct" in some prescribed fraction of the trials. Here "correct" simply means that his judgments are consistent.

In terms of the model, localization judgments are based on a comparison of the number of cells responding in the ipsilateral and contralateral accessory nuclei populations. The model is inherently probabilistic, so that repeated presentations of the same stimulus configuration will result in different numbers of cells firing to each presentation. Thus far we have been interested in the average number of cells responding in each population. To obtain a measure of resolution we must consider the variability of the number of cells responding.

The way that we have chosen to treat this problem is to obtain from our empirical data a measure of the difference between the number of cells in the ipsilateral accessory nucleus and the number of cells in the contralateral accessory nucleus firing in response to a single stimulus presentation with a given interaural time or intensity difference, and then to determine by how much the time or intensity difference would have to be changed in order for the resulting difference between the numbers of cells on the two sides to be altered reliably from the original condition. (Under some conditions, this criterion of difference between numbers of cells responding at the two sides is not the same as the criterion of relative response activity at the two sides, R_I, that we used previously. If the original interaural time or intensity difference is zero, the two criteria are equivalent. If the original interaural time or intensity difference is not zero, the two criteria are, in general, not equivalent. We selected the criterion of difference between the numbers of cells responding at the two sides for this section because it is much more tractable analytically and because it gives results that in most cases of interest are indistinguishable from results obtained by using the criterion of relative response activity at the two sides. A discussion of the conditions under which the two criteria are equivalent is given in Appendix B.) We need some measure of reliability, just as we need such a measure to obtain just-noticeable difference values from psychophysical experiments. Here our measure will be that the difference between the numbers of cells

responding at the two sides be higher for one or the other stimulus condition in at least 75 per cent of the stimulus presentations.

In comparing the results of psychophysical experiments with predictions of the model, we must bear in mind that our data can tell us nothing about the unspecified higher centers of the model. These higher centers could play an important role in the discrimination of small changes of interaural time or intensity difference. We therefore should not expect a direct parallel between results of psychophysical experiments and the predictions of the model. What we can do is set an upper bound on the precision afforded by the model. If the system actually worked in this way, that is, if the judgment of sidedness were based only on the difference between the numbers of cells responding at the ipsilateral and contralateral accessory nuclei, then the higher centers could do no better than the predictions of the model. If the model predicts minimum detectable changes of interaural time or intensity difference that are as small as or smaller than comparable psychophysical results, we can conclude that the model has not been proved invalid.

10.2 ASSUMPTIONS

The minimum detectable change in interaural time or intensity difference afforded by the model is a function of the number of cells in the ipsilateral and contralateral accessory nuclei, the probability of firing of these cells, and the amount by which the probability of firing of these cells changes with a given change of interaural time or intensity difference. In order to obtain a measure of the precision afforded by the model, we assume that there is some number N of cells in the ipsilateral accessory nucleus and an equal number N of cells in the contralateral accessory nucleus.

To keep the discussion simple, we shall first assume that each accessory nucleus has a single homogeneous population of cells involved in binaural lateralization. Then we shall remove this restriction when we generalize the discussion to include the properties of many different cells.

Our data appear in the form of relative frequency of firing of individual cells. We assume that the probability of firing of an individual cell is equal to the observed relative frequency of firing of the cell (see Appendix A) and that the ensemble-average probability of firing of all cells in the population is equal to the time-average probability of firing of the one cell that we observed.

As in Section VIII, we assume that the firing of any given cell is statistically independent of the firing of all other cells (that is, that the activity of a cell is not affected by the activity of other cells), and we assume that the system is symmetrical.

10.3 DEFINITIONS AND COROLLARIES

The probability of firing of cells in the ipsilateral accessory nucleus is equal to P_I, and the probability of firing of cells in the contralateral accessory nucleus is equal to P_C.

The number of cells in the ipsilateral accessory nucleus responding to a given

stimulus presentation is a random variable denoted by X_I, and the number of cells in the contralateral accessory nucleus responding to a given stimulus presentation is a random variable denoted by X_C.

We define a random variable X_D as the difference between the number of cells responding in the ipsilateral accessory nucleus and the number responding in the contralateral accessory nucleus.

$$X_D = X_I - X_C. \tag{1}$$

We can make the following statements about the expected values of X_I, X_C, and X_D:

$$E(X_I) = NP_I \tag{2}$$

$$E(X_C) = NP_C \tag{3}$$

$$E(X_D) = E(X_I) - E(X_C) = N(P_I - P_C). \tag{4}$$

Because firings of individual cells are statistically independent, we can make the following statements about the variances of X_I, X_C, and X_D:

$$\sigma^2(X_I) = NP_I(1-P_I) \tag{5}$$

$$\sigma^2(X_C) = NP_C(1-P_C) \tag{6}$$

$$\sigma^2(X_D) = \sigma^2(X_I) + \sigma^2(X_C) = N[P_I(1-P_I)+P_C(1-P_C)]. \tag{7}$$

Equations 4 and 7 give the mean and variance of the distribution of differences between the number of cells responding to a single stimulus presentation in the ipsilateral accessory nucleus and the number responding in the contralateral accessory nucleus expressed in terms of the probability of firing of individual nerve cells. Now let us suppose that P_I is changed by a small amount ΔP_I and P_C is changed by a small amount ΔP_C. These changes could come about as a result of a small change in either interaural time difference or interaural intensity difference. We shall denote by X'_D the new random variable corresponding to the difference between the number of cells responding in the ipsilateral accessory nucleus and the number responding in the contralateral accessory nucleus. By analogy with Eqs. 4 and 7, we have

$$E(X'_D) = N[(P_I+\Delta P_I)-(P_C+\Delta P_C)] \tag{8}$$

and

$$\sigma^2(X'_D) = N[(P_I+\Delta P_I)(1-(P_I+\Delta P_I)) + (P_C+\Delta P_C)(1-(P_C+\Delta P_C))]. \tag{9}$$

Let us assume that the change between X_D and X'_D is such that the expected value of X'_D is greater than the expected value of X_D. In terms of the model, this change

would correspond to a movement of the virtual image toward the contralateral side. We ask by how much P_I and P_C would have to change in order that the probability that a single sample taken from the X'_D distribution be larger than a single sample taken from the X_D distribution be greater than 0.75. (If the higher centers in the model made a "forced-choice" decision of movement to the ipsilateral or contralateral side based simply on whether X'_D was less than or greater than X_D, the choice of 0.75 probability would mean that three out of four sets of stimulus presentations would result in the judgment "second click more to the contralateral side than first click." The choice of 0.75 is arbitrary. It is chosen as a convenient level midway between 0.5 (pure chance), and the asymptotic value 1.0 (perfect discrimination). Although it is chosen on much the same bases as the 0.75 level is chosen in psychophysical experiments, the result should not be construed as corresponding to a behavioral just-noticeable difference.)

The distribution of differences between X'_D and X_D has an expected value equal to the difference between the expected values of X'_D and X_D and a variance equal to the sum of the variances of X'_D and X_D, because of statistical independence of X'_D and X_D.

$$E(X'_D - X_D) = E(X'_D) - E(X_D) = N(\Delta P_I - \Delta P_C) \tag{10}$$

$$\begin{aligned}\sigma^2(X'_D - X_D) &= \sigma^2(X'_D) + \sigma^2(X_D) \\ &= N[(P_I+\Delta P_I)(1-(P_I+\Delta P_I))+(P_C+\Delta P_C)(1-(P_C+\Delta P_C))+P_I(1-P_I)+P_C(1-P_C)].\end{aligned} \tag{11}$$

For small ΔP_I and ΔP_C, Eq. 11 can be approximated by

$$\sigma^2(X'_D - X_D) \approx 2N[P_I(1-P_I) + P_C(1-P_C)]. \tag{12}$$

If N is large, we can approximate the distribution of $(X'_D - X_D)$ by a normal distribution, and from a tabulation of the normal distribution we find that

$$P[(X'_D - X_D) > 0] > 0.75 \qquad \text{if } E(X'_D - X_D) > 0.7\,\sigma(X'_D - X_D). \tag{13}$$

Setting $E(X'_D - X_D) = 0.7\sigma(X'_D - X_D)$ and substituting from Eqs. 10 and 12, we have

$$N(\Delta P_I - \Delta P_C) = 0.7\sqrt{2N[P_I(1-P_I) + P_C(1-P_C)]} \approx \sqrt{N[P_I(1-P_I) + P_C(1-P_C)]}. \tag{14}$$

Equation 14 can be used to determine the precision afforded by the model in detecting small changes in interaural time or intensity difference, under the simplifying assumption that one cell that we observed is representative of all cells in the accessory nucleus. We can obtain P_I and P_C from our data. Given P_I and P_C, and assuming a value for N, we can use Eq. 14 to determine the minimum change in P_I and P_C that meets our criterion for "detectability." Given this change in P_I and P_C, we can determine the corresponding change in interaural time or intensity difference by linear interpolation

of the experimental results.

The generalization of Eq. 14 to include the activity of many different cells parallels the generalization of R_I to include the activity of many different cells (section 8.2). If we assume that there are N cells in each accessory nucleus, and we have data on k cells, then we assume that each cell on which we have data is representative of a subpopulation of n = N/k cells. If we indicate the probability of response of the cells in the i^{th} subpopulation in the ipsilateral accessory nucleus by P_{Ii}, and the probability of response of the cells in the i^{th} subpopulation in the contralateral accessory nucleus by P_{Ci}, then Eq. 14 becomes

$$\sum_{i=1}^{k} (\Delta P_{Ii} - \Delta P_{Ci}) \approx \sqrt{\sum_{i=1}^{k} \left[\frac{P_{Ii}(1-P_{Ii}) + P_{Ci}(1-P_{Ci})}{N/k} \right]}. \qquad (15)$$

Let us set N = 5000. This estimate is based on the density of cells in the accessory nucleus and the size of the accessory nucleus,[61] and on the assumption that from one-fourth to one-half of the cells in the accessory nucleus are of the type that can be included in the model. The estimate is probably conservative.

10.4 RESULTS

The results for minimum detectable change in interaural time difference are presented in Fig. 41. Three overlapping intensity ranges are covered by cell groups A, B, and C of Section IX. We have computed two sets of results. For one set, P_{Ii} and P_{Ci} were taken from the condition $\Delta\tau$ = 0 μsec, and the relationships between ΔP_{Ii} and ΔP_{Ci} and change in $\Delta\tau$ were determined by linear interpolation between the conditions $\Delta\tau$ = +125 μsec and $\Delta\tau$ = −125 μsec. For the second set, P_{Ii} and P_{Ci} were taken from the conditions $\Delta\tau$ = +125 μsec and $\Delta\tau$ = −125 μsec, and the relationships between ΔP_{Ii} and ΔP_{Ci} and changes in $\Delta\tau$ were determined by linear interpolation between the conditions $\Delta\tau$ = 0 μsec, and $\Delta\tau$ = +250 μsec, and by linear interpolation between the conditions $\Delta\tau$ = 0 μsec and $\Delta\tau$ = −250 μsec. This is analogous to two psychophysical experiments, one in which the interaural time difference is initially set at 0 μsec and one in which the interaural time difference is initially set at 125 μsec.

The results are not inconsistent with results from human psychophysics. The minimum detectable change in interaural time difference predicted by the model is in the range 5-10 μsec, considerably smaller than the analogous results with humans.[45] Von Békésy[60] and Mills[43] both report that the minimum detectable change in interaural time difference increases only very slowly with increasing initial interaural time difference for an initial interaural time difference of less than 500 or 600 μsec. This point is not at all clear in terms of the model. The most that we can say is that the minimum detectable change in interaural time difference afforded by the model increases in seven out of ten cases as the initial interaural time difference increases from 0 μsec to 125 μsec. Comparisons across intensity within a single cell group are legitimate;

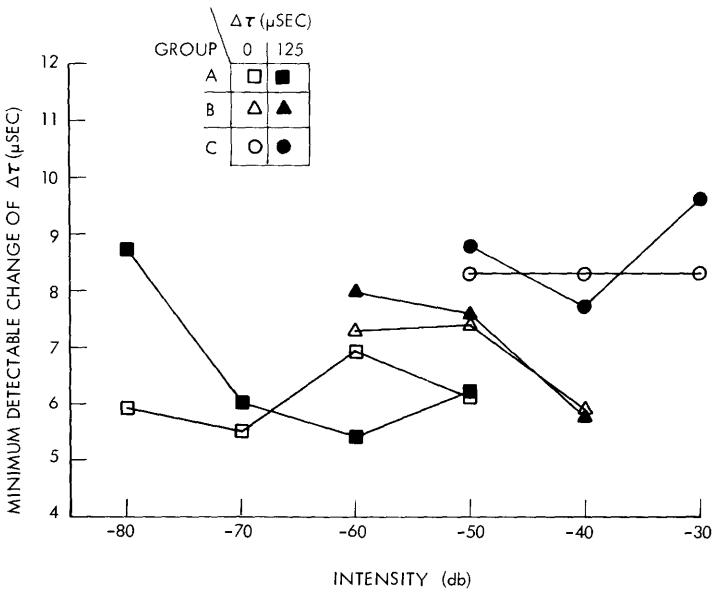


Fig. 41. Minimum detectable change in $\Delta\tau$ predicted by the model.

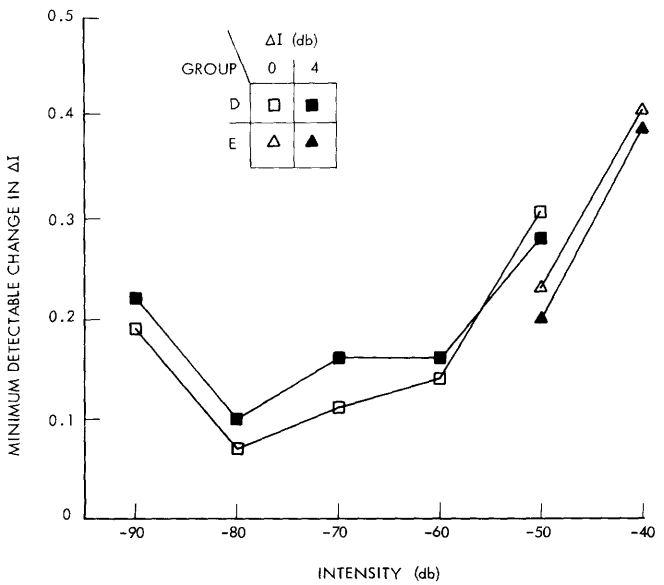


Fig. 42. Minimum detectable change in ΔI predicted by the model.

comparisons between one group and another are not – because different cells make up the sample. Bearing this in mind, we see that the model predicts no significant dependence of minimum detectable change of interaural time difference on intensity.

The results for minimum detectable change of interaural intensity difference are presented in Fig. 42. Two partially overlapping intensity ranges are covered by cell groups D and E of Section IX. As with interaural time difference, we computed two sets of results. For one set, P_{Ii} and P_{Ci} were taken from the condition $\Delta I = 0$ db, and the relationships between ΔP_{Ii} and ΔP_{Ci} and change in ΔI were determined by linear interpolation between the conditions $\Delta I = +4$ db and $\Delta I = -4$ db. For the second set, P_{Ii} and P_{Ci} were taken from the conditions $\Delta I = +4$ db and $\Delta I = -4$ db, and the relationships between ΔP_{Ii} and ΔP_{Ci} and change in ΔI were determined by linear interpolation between the conditions $\Delta I = 0$ db and $\Delta I = +8$ db and by linear interpolation between the conditions $\Delta I = 0$ db and $\Delta I = -8$ db. These would correspond to psychophysical experiments with initial interaural intensity difference set at 0 db and 4 db, respectively.

The minimum detectable change in interaural intensity difference predicted by the model ranges from less than 0.1 db to approximately 0.4 db, the value depending on average intensity. There are few analogous psychophysical data from experiments on humans. One experimenter[44] reports a just-noticeable difference with pure tones at an intensity of 50 db above threshold ranging from approximately 0.5 db to 1.0 db, as a function of frequency of the tone. There is a pronounced relationship between intensity and minimum detectable change in interaural intensity difference afforded by the model. The minimum detectable change in interaural intensity difference predicted by the model decreases with decreasing intensity down to an intensity of -80 db but increases slightly at an intensity of -90 db. Preliminary experiments from our laboratory[79] show a corresponding trend in one subject out of three investigated. Upton[80] reports that the minimum detectable interaural intensity difference for 800-cps tone bursts is highest (approximately 5 db) near threshold, reaches a minimum of approximately 0.75 db at moderate intensities, and increases to approximately 2 db at high intensities.

XI. CONCLUSIONS

11.1 SUMMARY OF RESEARCH

Our interest has been in the relationship between sensory performance and patterns of cell activity in the central nervous system: We wished to investigate the way in which sensory information is encoded for processing in the central nervous system. The aspect of sensory performance that we considered is the binaural localization of sounds. We attempted to relate results of psychophysical experiments on humans to results of electrophysiological experiments on cats. This strategy relies heavily on the assumption that the mechanisms of binaural localization in cat and man are similar. This assumption is by no means certain, but the limited evidence that we have indicates that it is likely.

We observed the electrical activity of single nerve cells in the auditory system of anesthetized cats by using binaurally presented clicks. Histological controls indicate that the cells that we observed are located in the accessory nucleus of the superior olive. We gave principal attention to cells that were excited by a click stimulus presented to the contralateral ear and inhibited by a click stimulus presented to the ipsilateral ear. This inhibition is manifested by a decrease in the percentage of stimulus presentations that evoke an action potential from the cell, and it is a function of interaural time difference, interaural intensity difference, and average intensity.

On the basis of these data we suggested a model for the process of localization of binaurally presented click stimuli. The model can be regarded as a logical "transducer" in which differences of intensity of the stimuli at the two ears and differences of arrival time of the stimuli are translated into different numbers of cells that respond in the ipsilateral and contralateral accessory nuclei. Information contained in the numbers of cells responding in the ipsilateral and contralateral accessory nuclei is utilized by unspecified "higher centers" and ultimately yields psychophysical judgments of sidedness.

The operations by which higher centers "compute" the judgment cannot be uniquely determined from the existing data. In this report we postulated two possible operations. (1) The degree of lateralization of the virtual image is related to the number of cells responding in the accessory nucleus on one side divided by the total number of cells responding in the accessory nuclei on both sides, a measure that we indicate by the symbol R_I. (2) The degree of lateralization of the virtual image is related to the difference between the number of cells responding in the accessory nucleus on one side and the number of cells responding on the other side. These are only two of many operations that could be postulated.

These two operations that we assumed (and all reasonable ones) become identical when attention is restricted to the conditions leading to a centered image, since a centered image would result from equal response activity in the two accessory nuclei. For other conditions, we would get different results if we postulated different operations.

The results of section 10.4, for example, would be unchanged if we postulated a different operation, since in that section we were concerned only with conditions leading to equal response activity in the two accessory nuclei. Questions such as the degree of lateralization of the virtual image resulting from a given interaural time or intensity difference, or the precision afforded by the model in detecting small changes of interaural time or intensity difference, would be affected.

Perhaps it is naive to try to formulate such a simple model. Perhaps the only way in which one can describe the results is to say that a given stimulus condition results in some unique pattern of activity in the central nervous system, and the possessor of the nervous system "learns" by "experience" to relate these patterns of activity to the physical world about him. If this were indeed the case, then the only relationship between patterns of neural activity and degree of lateralization of the virtual image would be an ad hoc, point-by-point relationship. One would hope that a more economical description is possible. The subject is, in any case, amenable to further investigation.

The model that we suggested is in many respects similar to models that have been proposed by other investigators. Van Bergeijk, in particular, suggested a model that is virtually identical to ours in that the lateralization of the virtual image is considered to be dependent on a comparison of response activity in the accessory nuclei on the two sides.[61] Our treatment differs from van Bergeijk's in that we have more concrete electrophysiological data on which to base our conjectures. Consequently, the detailed effects of interaural time and intensity differences at the level of the individual nerve cell are dissimilar.

Von Békésy's model for binaural localization,[60] described in section 5.3, is not incompatible with ours. As pointed out by van Bergeijk, the only change that needs to be made is to identify "neurons tuned to the left" and "neurons tuned to the right," in von Békésy's model, with "neurons responding in the left accessory nucleus" and "neurons responding in the right accessory nucleus."

The various "cortical" models for binaural localization described in section 5.2 are not incompatible with ours because we are concerned with different levels of neural activity. It may very well be, for example, that an imbalance between the stimuli presented to the two ears results in a larger evoked response at one cortical hemisphere than at the other. Our concern in this report has been with mechanisms at less central stations than the auditory cortex.

Other models are less easy to reconcile with ours. The "coincidence detector" suggested by Jeffress[62] and reviewed in section 5.4 can be regarded as a transducer that translates interaural time and intensity differences into site of neural activity at some station in the central nervous system. This is a different operation from the one that we have suggested, and would require response characteristics of individual nerve cells which are different from those that we observed. We have seen cells that show the highest relative frequency of response for nearly identical ipsilateral and contralateral

stimuli. This property is closer to that required by the Jeffress model than the properties of the time-intensity trading cells that we considered. We did not attempt a model based on these "summating" cells.

There is still one other model that can be contrasted with ours. This is the model suggested by Erulkar[21] and less explicitly by Hind et al.,[22] in which the localization judgment is related not to the number of cells firing but rather to the latency of response. Since we did not routinely measure latencies, we are not in a position to discuss this model in detail. There is, in general, a high correlation between latency of response and relative frequency of firing, and thus the two models might be expected to yield similar predictions.

In order to draw comparisons between predictions of the model and results of psychophysical experiments involving the presentation of binaural click stimuli to human observers, we applied to the model empirical data on the activity of single nerve cells in response to clicks presented to the two ears with combinations of interaural time difference, interaural intensity difference, and average intensity such that the same stimuli, if presented to a human observer, would lead to a judgment of a fused virtual image. Predictions of the model are not inconsistent with results of psychophysical experiments on humans.

If clicks are presented with 0-db interaural intensity difference and the interaural time difference is varied, the model predicts that the virtual image should be localized toward the side receiving earlier stimulation and that the amount of shift from the median plane should be related monotonically to the amount of interaural time difference. If clicks are presented with zero interaural time difference and the interaural intensity difference is varied, the model predicts that the virtual image should be localized toward the side receiving more intense stimulation and that the amount of shift should be related monotonically to the amount of interaural intensity difference. Both of these predictions are in agreement with available psychophysical data.

If clicks are presented with 5-db interaural intensity difference and the interaural time difference is varied, we obtain from the model a time-intensity trading relationship that indicates that equal response activity results at the two accessory nuclei when the click to one ear is more intense and the click to the other ear arrives earlier. The relationship between interaural time difference and interaural intensity difference for equal response activity at the two accessory nuclei decreases from approximately 90 μsec/db at low average intensity to approximately 15 μsec/db at high average intensity. This parallels results from human centering experiments, in which an interaural time difference is opposed to an interaural intensity difference to obtain a centered virtual image.

By means of some elementary statistics, we obtained a measure of the minimum detectable changes in interaural time and intensity difference afforded by the model. We obtain figures of 5-10 μsec for changes in interaural time difference, and 0.1-0.4 db for changes in interaural intensity difference. These figures are based on the assumption

that "higher" centers work on "noisy" data from the accessory nuclei and are thus limited even if they operate as ideal detectors. Results from the model therefore can only be construed as setting a bound on the performance of the over-all system. With this qualification, results from the model are in agreement with results from just-noticeable difference experiments with humans.

There are other results from the model for which comparable experimental data from psychophysics do not exist. These results can be regarded as predictions of the model and are subject to test by psychophysical experiments.

Comparison of results from the condition in which clicks are presented with nonzero interaural time difference and zero interaural intensity difference with those from the condition in which clicks are presented with nonzero interaural intensity difference and zero interaural time difference indicates that the degree of lateralization effected by a given interaural time difference should be independent of average intensity, but that the degree of lateralization effected by a given interaural intensity difference should increase as the average intensity decreases. (This interpretation is based on one possible operation by the higher centers, that the degree of lateralization of the virtual image is determined by the amount of response activity in one accessory nucleus divided by the total amount of response activity in both accessory nuclei.) The few psychophysical data that deal with the effect of interaural time difference and average intensity are inconclusive.

The minimum detectable change in interaural time difference predicted by the model appears to be independent of average intensity, and the minimum detectable change in interaural intensity difference appears to increase as the average intensity decreases. (This interpretation is based on the measure of difference between the amount of response activity in the two accessory nuclei.) Some psychophysical experiments tend to support this prediction, although others indicate that this prediction is incorrect.

11.2 SUGGESTIONS FOR FURTHER RESEARCH

The present study has indicated that a model of the type considered can be used to relate electrophysiological findings in the cat to some aspects of binaural localization of sounds in humans. The domain of applicability of the model is still quite restricted, and our assumption that in this respect the auditory systems of cat and man are comparable remains to be verified.

The only parameters of click stimulation that we explored are interaural time difference, interaural intensity difference, and average intensity. Both from the point of view of extending the domain of applicability of the model and from the point of view of investigating the physiological mechanisms governing the activity of these cells, it would be desirable to use a less restricted class of stimuli. As a specific example, preliminary observations indicate that continuous white noise added to a click stimulus produces some quite complex effects. The responsiveness of cells in the accessory nucleus to pure tones, tone bursts, and bursts of narrow-band noise should also be investigated.

By considering the model, we made a number of predictions about results of psychophysical experiments on humans. These predictions relate to the outcome of experiments determining the position of the virtual image as a function of interaural time difference, interaural intensity difference, and average intensity, and to the outcome of experiments determining the minimum detectable changes in interaural time and intensity difference as a function of these same three parameters. Existing results enabled us to conclude that there is reasonable correspondence between predictions based on the model and results of psychophysical experiments on humans, but there are many areas in which the corresponding psychophysical data do not exist. An appropriately designed series of psychophysical experiments could provide valuable information on the range of validity of the model.

There remains the question of the degree to which cats and humans are comparable in tasks requiring binaural localization of sounds. Some behavioral experimentation has been carried out on cats, but in every case the stimulus has been delivered through a loud-speaker. We therefore are unable to make any statement about the relative contribution of interaural time difference and interaural intensity difference to the lateralization of acoustic stimuli. If it were possible to devise some sort of earphone that a cat would tolerate, we might be able to obtain a more satisfactory answer to this question.

APPENDIX A

RELATIVE FREQUENCY OF FIRING AS AN ESTIMATOR FOR PROBABILITY OF FIRING

We assume that the activity of the nerve cell in question can be described by a probability of firing for a given stimulus configuration, and we would like to obtain an estimate of this probability from our data. We have available a sample of 50 stimulus presentations, giving the relative frequency of firing P. We are using this as an estimator of the probability of firing. It can be shown (cf. a text on statistics, for example Freund[81]) that if we were to repeat the experiment many times over, the value obtained for P would on the average be equal to the probability of firing (that is, P is an unbiased estimator of the probability of firing).

We would also like to know how close the relative frequency of firing that we determine on the basis of 50 stimulus presentations is to the probability of firing. In other words, we are interested in the variability of the estimator, as well as its mean. This can be determined by reference to a tabulation of the binomial distribution. Following, for purposes of reference, are a few characteristic numbers: If the probability of firing is 0.5, in 9 out of 10 samples of 50 stimulus presentations the relative frequency will be between 0.38 and 0.62; in 99 out of 100 samples it will be between 0.32 and 0.68. If the probability is 0.25, then in 9 out of 10 samples the relative frequency will be between 0.16 and 0.36; in 99 out of 100 samples it will be between 0.10 and 0.42. If the probability is 0.1, then in 9 out of 10 samples the relative frequency will be between 0.04 and 0.18; in 99 out of 100 samples it will be between 0.00 and 0.22.

APPENDIX B

CONDITIONS UNDER WHICH THE CRITERION OF RELATIVE RESPONSE ACTIVITY R_I IS EQUIVALENT TO THE CRITERION OF DIFFERENCE BETWEEN NUMBER OF CELLS RESPONDING AT THE TWO SIDES

The number of cells in the ipsilateral accessory nucleus firing in response to an initial stimulus presentation is a random variable X_I, and the number of cells in the contralateral accessory nucleus firing in response to this same stimulus presentation is a random variable X_C. The numbers of cells in the ipsilateral and contralateral accessory nuclei firing in response to a second stimulus presentation are $X'_I = X_I + \Delta X_I$ and $X'_C = X_C + \Delta X_C$, respectively.

Two criteria for discrimination of the two stimulus presentations are (1) that X_D, the difference between the numbers of cells in the two accessory nuclei firing in response to the initial stimulus presentation (that is, $X_D = X_I - X_C$) differ from X'_D, the difference between the numbers of cells in the two accessory nuclei firing in response to the second stimulus presentation (that is, $X'_D = X'_I - X'_C$); and (2) that $\underline{R}_I$, the relative number of cells in the ipsilateral and contralateral accessory nuclei firing in response to the initial stimulus presentation $\left(\text{that is, } \underline{R}_I = \frac{X_I}{X_I + X_C}\right)$, differ from $\underline{R}'_I$, the relative number of cells in the two accessory nuclei firing in response to the second stimulus presentation $\left(\text{that is, } \underline{R}'_I = \frac{X'_I}{X'_I + X'_C}\right)$, where the underline is used to distinguish $\underline{R}_I$ and $\underline{R}'_I$ from R_I, the <u>average</u> relative amount of response activity in the two accessory nuclei. R_I is a number; $\underline{R}_I$ and $\underline{R}'_I$ are random variables.

Let us assume that $X'_D \geq X_D$. We wish to determine the conditions under which $R'_I \geq R_I$.

Since

$$\underline{R}_I = \frac{X_I}{X_I + X_C} \tag{B-1}$$

and

$$\underline{R}'_I = \frac{X'_I}{X'_I + X'_C} = \frac{X_I + \Delta X_I}{X_I + \Delta X_I + X_C + \Delta X_C}, \tag{B-2}$$

it follows that a condition equivalent to $\underline{R}'_I$ being equal to or greater than $\underline{R}_I$ is that $\frac{\Delta X_I}{X_I}$, the fractional change in the numerator, be equal to or greater than $\frac{\Delta X_I + \Delta X_C}{X_I + X_C}$, the fractional change in the denominator.

$$[\underline{R}'_I \geq \underline{R}_I] \Longleftrightarrow \left[\frac{\Delta X_I}{X_I} \geq \frac{\Delta X_I + \Delta X_C}{X_I + X_C}\right]. \tag{B-3}$$

If the sum of ΔX_I and ΔX_C is equal to or greater than zero, relation (B-3) can be rewritten

$$\frac{\Delta X_I}{\Delta X_I + \Delta X_C} \geq \frac{X_I}{X_I + X_C} = \underline{R}_I. \tag{B-4}$$

If the sum of ΔX_I and ΔX_C is equal to or less than zero, then relation (B-3) can be rewritten

$$\frac{\Delta X_I}{\Delta X_I + \Delta X_C} \leq \frac{X_I}{X_I + X_C} = \underline{R}_I. \tag{B-5}$$

It follows from the definitions that

$$[X'_D \geq X_D] \Longleftrightarrow [\Delta X_I \geq \Delta X_C]. \tag{B-6}$$

There are a number of ways in which X_I and X_C can change so that $\Delta X_I \geq \Delta X_C$:

(i) $\Delta X_I \geq 0$, $\Delta X_C = 0$;

(ii) $\Delta X_I = 0$, $\Delta X_C \leq 0$;

(iii) $\Delta X_I \geq 0$, $\Delta X_C \leq 0$, $|\Delta X_I| \geq |\Delta X_C|$;

(iv) $\Delta X_I \geq 0$, $\Delta X_C \leq 0$, $|\Delta X_C| \geq |\Delta X_I|$;

(v) $\Delta X_I \geq 0$, $\Delta X_C \geq 0$, $|\Delta X_I| \geq |\Delta X_C|$;

(vi) $\Delta X_I \leq 0$, $\Delta X_C \leq 0$, $|\Delta X_C| \geq |\Delta X_I|$. We shall consider these six cases individually.

(i) Equation B-4 applies. $\frac{\Delta X_I}{\Delta X_I + \Delta X_C}$ is equal to unity, which is the least upper bound of $\underline{R}_I$. The inequality of (B-4) is satisfied in every case.

(ii) Equation B-5 applies. $\frac{\Delta X_I}{\Delta X_I + \Delta X_C}$ is equal to zero, which is the greatest lower bound of $\underline{R}_I$. The inequality of (B-5) is satisfied in every case.

(iii) Equation B-4 applies. $\frac{\Delta X_I}{\Delta X_I + \Delta X_C} \geq 1$. The inequality of (B-4) is satisfied in every case.

(iv) Equation B-5 applies. $\frac{\Delta X_I}{\Delta X_I + \Delta X_C} \leq 0$. The inequality of (B-5) is satisfied in every case.

(v) Equation B-4 applies. $\frac{\Delta X_I}{\Delta X_I + \Delta X_C} \geq 0.5$, so that in general the inequality of (B-4) is satisfied only if $\underline{R}_I$ is equal to or less that 0.5.

(vi) Equation B-5 applies. $\frac{\Delta X_I}{\Delta X_I + \Delta X_C} \leq 0.5$, so that in general the inequality of (B-5) is satisfied only if $\underline{R}_I$ is equal to or greater than 0.5.

The results in conditions (i)-(vi) can be reformulated and summarized as follows: If $\underline{R}_I$ is equal to 0.5 (that is, if in the initial condition there is equal response activity in the two accessory nuclei), then the two criteria for discrimination are in every case equivalent. If $\underline{R}_I$ is not equal to 0.5 (that is, if in the initial condition there is not equal response activity in the two accessory nuclei), then the two criteria in general are not equivalent.

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